NELI MURAKI ISHIKAWA

VALIDAÇÃO DO FACT-F NO BRASIL E AVALIAÇÃO DA FADIGA E QUALIDADE DE VIDA EM MULHERES COM CÂNCER DE MAMA

Tese de Doutorado

ORIENTADOR: Profª. Drª. SOPHIE FRANÇOISE MAURICETTE DERCHAIN
CO-ORIENTADOR: Prof. Dr. LUIZ CLAUDIO SANTOS THULER

Unicamp
2009

NELI MURAKI ISHIKAWA

VALIDAÇÃO DO FACT-F NO BRASIL E AVALIAÇÃO DA FADIGA E QUALIDADE DE VIDA EM MULHERES COM CÂNCER DE MAMA

Tese de Doutorado apresentada à Pós-Graduação da Faculdade de Ciências Médicas da Universidade Estadual de Campinas para obtenção do Título de Doutor em Tocoginecologia, área de Ciências Biomédicas.

ORIENTADOR: Profª. Drª. SOPHIE FRANÇOISE MAURICETTE DERCHAIN
CO-ORIENTADOR: Prof. Dr. LUIZ CLAUDIO SANTOS THULER

Unicamp
2009

FICHA CATALOGRÁFICA ELABORADA PELA
BIBLIOTECA DA FACULDADE DE CIÊNCIAS MÉDICAS
UNICAMP
Bibliotecário: Sandra Lúcia Pereira – CRB-8ª / 6044

Is3v

Ishikawa, Neli Muraki
Validação do FACT – F no Brasil e avaliação da fadiga e qualidade de vida em mulheres com câncer de mama / Neli Muraki Ishikawa. Campinas, SP : [s.n.], 2009.

Orientadores: Sophie Françoise Mauricette Derchain, Luiz Cláudio Santos Thuler
Tese (Doutorado) Universidade Estadual de Campinas. Faculdade de Ciências Médicas.

1. Questionários. 2. Quimioterapia. 3. Qualidade de vida. 4. Fadiga. 5. Reprodutibilidade dos testes. 6. Mamas – câncer. 7. Validação. I. Derchain, Sophie Françoise Mauricette. II. Thuler, Luiz Cláudio Santos. III. Universidade Estadual de Campinas. Faculdade de Ciências Médicas. IV. Título.

Título em inglês: Validation of FACT-F in Brazil and evaluation of fadigue and quality of life in women with breast cancer
Keywords:
- Questionnaires
- Drug therapy
- Quality of life
- Fatigue
- Reproducibility of results
- Neoplasm, breast
- Validation

Titulação: Doutor em Tocoginecologia
Área de concentração: Ciências Biomédicas

Banca examinadora:
Prof. Dr. Luiz Cláudio Santos Thuler
Prof. Dr. Luis Otávio Zanatta Sarian
Profa. Dra. Maria José Martins Duarte Osis
Prof. Dr. Nivaldo Antonio Parizotto
Profa. Dra. Telma Guarisi

Data da defesa: 16 – 01 – 2009

Diagramação e arte final: Assessoria Técnica do CAISM (ASTEC)

BANCA EXAMINADORA DA TESE DE DOUTORADO

Aluno: NELI MURAKI ISHIKAWA

Orientador: Profª. Drª. SOPHIE FRANÇOISE MAURICETTE DERCHAIN

Co-Orientador: Prof. Dr. LUIZ CLAUDIO SANTOS THULER

Membros:

1. Luiz Claudio Santos Thuler
2.
3.
4.
5.

Curso de Pós-Graduação em Tocoginecologia da Faculdade de Ciências Médicas da Universidade Estadual de Campinas

Data: 16/01/2009

Dedico este trabalho...

ao meu pai Soiti (in memoriam),
a minha mãe Kimiko,
ao meu marido Edison,
a minha filha Helena,
aos meus irmãos,
aos pacientes,
e amigos.

Agradecimentos

A Deus, por me dar a certeza de que sempre existe um caminho.

À Profª Drª Sophie Françoise Mauricette Derchain, a quem tenho como exemplo de amor à profissão e à arte de ensinar. Minha admiração e meus agradecimentos pelas orientações relevantes e disposição em me receber e ajudar ao longo deste estudo.

Ao Prof Dr Luiz Cláudio Santos Thuler, a quem tenho grande admiração por sua integridade pessoal, capacidade de trabalho, meus especiais agradecimentos pela sua valiosa orientação e ensinamentos no decorrer desses anos no INCA.

À Profª Drª Maria José Martins Duarte Osis e ao Prof Dr. Luis Otávio Zanatta Sarian, pelas críticas e sugestões no processo de qualificação.

Aos meus colaboradores deste estudo: Dra. Alessandra Grasso Giglio, Dra.Clarissa Seródio da Rocha Baldotto, Dr. Carlos José Coelho de Andrade, Dr. Luiz Guilherme Pinheiro Branco, e às enfermeiras Eli Yanase, Maria de Fátima Rodrigues B. Ventura, pela cooperação e concretização deste estudo, permitindo um trabalho em equipe.

A toda a equipe do Serviço de Oncologia e equipe de Enfermagem do Serviço de Oncologia Clínica e Quimioterappia do HC1 e HC3, pela colaboração na realização deste estudo.

Aos amigos do INCA que foram alunos do mestrado na UNICAMP, pelas boas lembranças, pelo bom convívio, pelo incentivo e apoio nessa caminhada pela pós-graduação na UNICAMP.

Ao Péricles Maranhão Neto pela revisão dos artigos da língua inglesa.

À estatística Sirlei Siani Morais pela revisão das análises estatísticas.

Ao Prof. Dr. Luiz Carlos Zeferino, pelo apoio na realização deste curso.

À Profª Drª Sheila Pereira da Silva e Souza, responsável anterior pela Coordenação de Ensino e Divulgação Científica (CEDC), do Instituto Nacional de Câncer (INCA), uma das mentoras da reunião de duas renomadas instituições de assistência / ensino / pesquisa.

Aos Professores-Doutores José Gomes Temporão e Luiz Antônio Santini Rodrigues da Silva, antigo e atual Diretor Geral do INCA, pelo cumprimento da política de ampliação dos quadros de mestres e doutores, e apoio na realização deste trabalho.

À Profª Drª Marisa Maria Dreyer Breitenbach, responsável pela Coordenação de Pesquisa (CPQ) do INCA, decisiva em muitos momentos.

À Profª Drª Eliana Cláudia de Otero Ribeiro, atual responsável pela CEDC do INCA, pelas aulas e posicionamento de apoio na responsabilidade institucional com seus profissionais.

À Srª Margarete Amado de Souza Donadon, secretária da Subcomissão de Pós-Graduação do Departamento de Tocoginecologia, da UNICAMP, pelo apoio e colaboração em tantos momentos.

A toda a equipe da Astec, pela colaboração na formatação do trabalho e pela correção deste material.

Aos pacientes, que mesmo atravessando um momento crucial de suas vidas, gentilmente concordaram em participar deste estudo.

A todos os amigos e funcionários do INCA, pelo incentivo na realização desta etapa de pós-graduação, cujos nomes deixo de citar, mas que se sentirão incluídos, meus sinceros agradecimentos.

Sumário

Símbolos, Siglas e Abreviaturas

AC – *Doxorubicin / cyclophosphamide*

CAF – *Cyclophosphamide ,/ doxorubicin / 5-fluorouracil*

CEF – *Cyclophosphamide / epirubicin / fluorouracil*

CMF – *Cyclophosphamide / methotrexate / 5-fluorouracil*

ECOG – *Eastern Cooperative Oncology Group*

EORTC QLQ C30 – *European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire*

EWB – *Emotional Well-Being*

FACIT – *Functional Assessment of Chronic Illness Therapy*

FACT – *Functional Assessment of Cancer Therapy*

FACT-Br – *Functional Assessment of Cancer Therapy - Brain cancer*

FACT-C – *Functional Assessment of Cancer Therapy - Colorectal cancer*

FACT-F – *Functional Assessment of Cancer Therapy- Fatigue*

FACT-G – *Functional Assessment of Cancer Therapy- General*

FACT-L – *Functional Assessment of Cancer Therapy- Lung cancer*

FACT-P – *Functional Assessment of Cancer Therapy - Prostate cancer*

FAHI – *Functional Assessment of Human Immunodeficiency Virus Infection*

FAMS – *Functional Assessment of Multiple Sclerosis*

FQ – *Fatigue Questionnaire*

FS – *Fatigue Subscale*

FWB – *Functional Well-being*

HRQOL – *Health Related Quality of Life*

ICC – *Intraclass Correlation Coefficient*

INCA – Instituto Nacional de Câncer

NCI – *National Cancer Institute*

P – Probabilidade da amostra

PS – *Performance Status*

PWB – *Physical Well-being*

QOL – *Quality of Life*

QV – Qualidade de vida

SD – *Standard Deviation*

SF-36 – *Short-Form Health Survey*

SWB – *Social/Family Well-being*

UNICAMP – Universidade Estadual de Campinas

Resumo

Objetivos: Validar a versão em português do questionário *Functional Assessment of Cancer Therapy-Fatigue (FACT-F)* em pacientes com câncer e avaliar a fadiga e a qualidade de vida em mulheres com câncer de mama em quimioterapia. **Sujeitos e métodos:** Para este estudo de validação do questionário FACT-F foram incluídos 270 pacientes, sendo 85 para avaliar a reprodutibilidade do questionário com diferentes tipos de câncer. Para avaliar a fadiga e qualidade de vida em mulheres com câncer de mama em quimioterapia foi realizado um estudo longitudinal e incluídas 188 mulheres. O período de realização dos estudos foi de setembro de 2005 a março de 2007. Inicialmente foi avaliada a reprodutibilidade do *FACT-F* através do teste-reteste para a língua portuguesa em pacientes com câncer; em seguida a versão para língua portuguesa foi submetida à validação, a fim de estabelecer propriedades incluindo a validade e confiabilidade em uma amostra de pacientes brasileiros com câncer; finalmente foi avaliada a relação entre fadiga e qualidade de vida relacionada à saúde em pacientes com câncer de mama antes do início da quimioterapia, e após 3º e 6º ciclo de quimioterapia. **Resultados:** O FACT-F apresentou uma boa correlação intraclasse para os domínios que foram de 0,72 para bem-estar físico; 0,91 para bem-estar social e familiar; 0,90 para

bem-estar emocional; 0,86 para bem-estar funcional; 0,88 para subescala fadiga e 0,91 para FACT-F. O coeficiente a de Cronbach foi de 0,78 para bem-estar físico; 0,68 para bem-estar social e familiar; 0,75 para bem-estar emocional; 0,74 para bem-estar funcional; 0,91 para subescala fadigas e 0,92 para o FACT-F. A correlação de Pearson foi excelente entre domínio vitalidade do SF-36 e FACT-F total (r=0,76), e subscala fadiga (r=0,77); sendo boa entre o FACT-F e na maioria dos domínios do SF-36, variando de r =0,51 a 0,76, exceto para domínio físico (r =0,31). Houve uma diminuição significante dos escores do FACT-F (p<0,001), FACT-G (p=0,029), subescala fadiga (p<0,001) e bem-estar físico (p<0,001) entre antes da quimioterapia e após o terceiro ciclo de quimioterapia e permanecendo um platô até após o sexto ciclo (p<0,001) refletindo uma manutenção da fadiga e baixa qualidade de vida em mulheres com câncer de mama. O escore do bem-estar emocional teve um pequeno aumento após o terceiro ciclo (p<0,001), permanecendo após o sexto ciclo (p<0,001) enquanto os escores do bem-estar funcional e do bem-estar social e familiar não mostraram diferença entre antes e durante a quimioterapia. A fadiga está relacionada à baixa qualidade de vida relacionada à saúde. **Conclusões:** O instrumento FACT-F apresentou uma boa reprodutibilidade teste-reteste em uma série heterogênea de pacientes, com diferentes tipos de câncer, *performance status* e estadiamento. A versão portuguesa do FACT-F é um instrumento válido e confiável para avaliar a fadiga e qualidade de vida em pacientes com câncer. A fadiga aumentou e piorou a qualidade de vida em pacientes com câncer de mama submetidas à quimioterapia.

Summary

Objectives: Validate the Portuguese version of the FACT-F questionnaire in cancer patients and fatigue and quality of life in breast cancer patients in chemotherapy. **Subjects and methods:** This study of FACT-F validation included 270 patients, 85 were to evaluate the questionnaire reproducibility in patients with different types of cancer. The study to evaluate fatigue and quality of life in breast cancer during chemotherapy was prospective and 188 women were included. The study was conducted from September 2005 to March 2007. It was initially assessed the reproducibility of the FACT-F through the test-retest for the Portuguese language in patients with cancer, following the Portuguese language version was submitted to validation in order to establish properties including the validity and reliability in a sample of Brazilian cancer patients, finally, it was assessed the relation between fatigue and quality of life related to health in patients with breast cancer before the start of chemotherapy, and after 3 and 6 cycle of chemotherapy. **Results:** FACT-F had a Intraclass Correlation Coefficient to the domains that were 0.72 for physical well-being, 0.91 for social/family well-being; 0.90 for emotional well-being, 0.86 for functional well-being, 0.88 fatigue subscale and 0.91 for total FACT-F. Cronbach a coefficient was 0.78 for physical well-being, 0.68 for

social/family well-being, 0.75 for emotional well-being, 0.74 for functional well-being, 0.91 for fatigue, and 0.92 for total FACT-F. The Pearson correlation was excellent between SF-36 vitality scale and total FACT-F (r=0.76) and fatigue subscale (r=0.77); and good correlation in most dimensions ranging from r=0.51 to r=0.76, except to SF-36 physical (r=0.31). There were a significant decrease in mean FACT-F ($p<0.001$), FACT-G ($p=0.029$), Fatigue subscale ($p<0.001$), Physical well being ($p<0,001$) scores between the start of the treatment and after cycle 3 and than appeared to plateau at cycle 6 ($p<0.001$) reflecting maintenance in fatigue symptoms and lower quality of life in breast cancer patients. The Emotional well being scores increased a little between the start of chemotherapy and after cycle 3 ($p<0.001$) and remained a plateau at cycle 6 ($p<0.001$) while social/family well-being scores showed no differences before and during chemotherapy. Fatigue is related to lower health related quality of life. **Conclusion:** FACT-F questionnaire in Portuguese has good test-retest reproducibility in patients with different types of cancer, performance status and stages. The Portuguese version of FACT-F is a reliable and valid instrument to assess QOL and fatigue to screen cancer-related fatigue in Brazilian cancer patients. Fatigue increased and worsened in health related HRQOL in breast cancer submitted to chemotherapy.

1. Introdução

O câncer de mama é um importante problema de saúde pública devido à sua alta incidência e mortalidade. No Brasil, as estimativas realizadas pelo Instituto Nacional de Câncer (INCA) para o ano de 2008, válidas também para o ano de 2009, apontam que ocorrerão 466.730 casos novos de câncer. Os tipos mais incidentes, à exceção do câncer de pele do tipo não melanoma, serão os cânceres de próstata e de pulmão, entre os homens, e os cânceres de mama e de colo do útero entre as mulheres, acompanhando o mesmo perfil da magnitude observada no mundo.

O número de casos novos de câncer de mama esperados para o Brasil, no ano de 2008, é de 49.400, com um risco estimado de 51 casos a cada 100 mil mulheres (INCA, 2007).

Na região Sudeste, o câncer de mama é o mais incidente entre as mulheres, com um risco estimado de 68 casos novos por 100 mil. Sem considerar os tumores de pele não melanoma, esse tipo de câncer também é o mais frequente nas mulheres das regiões Sul (67/100.000), Centro-Oeste (38/100.000) e Nordeste (28/100.000). Na região Norte é o segundo tumor mais incidente (16/100.000).

Apesar de ser considerado um câncer de relativamente bom prognóstico, as taxas de mortalidade por câncer de mama continuam elevadas no Brasil, muito provavelmente porque a doença ainda é diagnosticada em estádios avançados (INCA, 2007).

Os avanços tecnológicos no diagnóstico e o tratamento precoce do câncer têm aumentado a sobrevida dos pacientes. Um dos maiores problemas relatados pelos pacientes com câncer é a fadiga. A fadiga é altamente prevalente, ocorrendo em até 94% dos pacientes com câncer. Sua frequência aumenta significativamente durante a quimioterapia e a radioterapia (Ishikawa et al., 2005).

Para a maioria dos indivíduos a fadiga é uma resposta protetora para o estresse físico e psicológico e o descanso restaura completamente o bem-estar no indivíduo saudável (Ahlberg et al., 2003). Os pacientes com fadiga se expressam utilizando os termos cansado, débil, extenuado, esgotado, farto, pesado ou lento. Os profissionais da saúde empregam termos como astenia, lassitude, prostração, intolerância ao exercício, falta de energia e fraqueza (NCI, 2008).

A fadiga é a maior causa da diminuição da qualidade de vida em pacientes com câncer (Curt, 2000). A fadiga relacionada ao câncer tem um impacto sobre a vida dos pacientes com devastadoras conseqüências econômicas e sociais, e podem persistir por meses ou mesmo anos após a conclusão do tratamento (Prue et al., 2006). Devido ao impacto da fadiga sobre a qualidade de vida do paciente, os estudos sobre os efeitos relacionados com o tratamento são de relevância para o tratamento do câncer (Visser e Smets, 1998).

A causa da fadiga é desconhecida. A explicação do mecanismo que promove a fadiga relacionada ao câncer ainda permanece obscura, mas como sintoma, é quase certo que a sua origem seja multifatorial (Stone e Minton, 2008). Acredita-se que haja fatores que contribuam para a fadiga como o próprio tratamento de câncer, anemia, fatores de nutrição, fatores psicológicos, fatores cognitivos, transtorno de sono e inatividade e medicamentos (NCI, 2008). A depressão, a incapacidade física, a necessidade de dormir e descansar durante o dia e a tendência de atribuir as queixas de fadiga ao tratamento de câncer de mama contribuem significativamente para a severidade da fadiga (Servaes et al., 2002). Embora muitos pacientes com câncer relatem que a fadiga é um obstáculo para manter as atividades normais diárias e com qualidade de vida, raramente é avaliado e tratado na prática clínica (Portenoy e Itri, 1999).

Dillon e Kelly (2003) realizaram um estudo na Irlanda sobre fadiga envolvendo 109 médicos e 160 enfermeiros que atendem pacientes oncológicos e 143 pacientes oncológicos. A maioria dos médicos e enfermeiros relatou que a náusea era o efeito colateral que mais incomodava os pacientes. A alopecia foi o segundo efeito colateral na percepção dos médicos e a fadiga foi o segundo na percepção dos enfermeiros. Em contrapartida, quase metade dos pacientes (41%) relataram que a fadiga era o efeito colateral que mais os afetava durante o tratamento, seguida por náusea com 12% e 8% a queda de cabelo. Esses achados sugeriram que os médicos e enfermeiros estavam subestimando o impacto da fadiga nos pacientes. Ambos os profissionais concordaram que os pacientes vivenciavam a fadiga e que os pacientes mencionaram a fadiga na maioria das visitas.

Em outro estudo realizado por Stone et al. (2003) sobre a fadiga relacionada ao câncer, entre profissionais de saúde, pacientes e cuidadores, os autores relataram que quando os pacientes dialogavam com o médico sobre a fadiga, os médicos referiam que a fadiga era causada pelo câncer (31%) e pelo tratamento de câncer (77%). Cinqüenta e dois por cento dos pacientes com fadiga nunca falaram sobre este sintoma com o médico, porque achavam que este sintoma era "inevitável", que não achavam "suficientemente importantes" e acreditavam que "nada podia ser feito" ou que os médicos também "nunca tocaram neste assunto". Dezesseis por cento dos pacientes que conversaram com os médicos sobre esse assunto relataram que "tinha que viver com isso" ou que "pouco poderia ser feito" para tratar a fadiga. Neste estudo, muitos profissionais de saúde (79%) acreditam que a fadiga pode ser causada pela combinação da doença e do tratamento, e 85% deles falaram aos pacientes que era um efeito colateral do câncer e/ou tratamento. Oitenta e sete por cento achavam que a fadiga foi subtratada. Os profissionais de saúde prescreveram ou recomendaram um tratamento para aproximadamente 50% dos pacientes com fadiga. As recomendações mais frequentes desses profissionais foram para descansar e relaxar, melhorar a dieta, transfusão sanguínea, fisioterapia e exercícios e prescrição de medicamentos. Muitos dos cuidadores dos pacientes envolvidos eram um familiar ou um amigo, e eles identificavam a fadiga como um problema importante para os pacientes, porém somente 26% dos cuidadores conversaram sobre a fadiga com o médico. E as razões mais frequentes foram porque eles acharam que era "inevitável" ou que "nada poderia ser feito".

A avaliação da fadiga tem sido amplamente utilizada para avaliar os efeitos dos tratamentos. É também útil nos estudos de novas abordagens e novas maneiras de controlar os sintomas, para melhorar o conhecimento dos médicos e identificar as necessidades dos pacientes, visando ao desenvolvimento de estratégias adequadas para o cuidado (Flechtner e Bottomley, 2003).

Em uma recente revisão sistemática da literatura científica foram encontradas 14 escalas para avaliar a fadiga, e os questionários mais comumente utilizados foram o *Functional Assessment of Cancer Therapy Fatigue* (FACT-F), o *European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire* subscala fadiga (EORTC QLQ C30) e o *Fatigue Questionnaire* (FQ) (Minton e Stone, 2008).

O Sistema de Medição Functional Assessment of Chronic Illness Therapy (FACIT), em desenvolvimento desde 1987, produziu a sua quarta versão, edição de novembro de 1997 (Webster et al., 1999). O sistema FACIT (Lent et al., 1999) inclui o Functional Assessment of Cancer Therapy (FACT), o Functional Assessment of Human Immunodeficiency Virus Infection (FAHI), e o Functional Assessment of Multiple Sclerosis (FAMS). O FACT-G (Cella et al., 1993) em combinação com a subescala "preocupações adicionais" fornece uma avaliação da qualidade de vida específica para vários tipos de cânceres, como próstata (FACT-P) (Esper et al., 1997), colorretal (FACT-C) (Ward et al., 1999), cerebral (FACT-Br) (Weitzner et al., 1995), pulmão (FACT-L) (Cella et al., 1995), e etc. Estes questionários foram desenvolvidos nos Estados Unidos e estão disponíveis em 45 idiomas, permitindo a comparação de diferentes populações, utilizando-se de um método rigoroso de

tradução e retro-tradução, testes psicométricos e entrevista cognitiva (Webster et al., 2003). Os questionários do sistema FACIT só podem ser utilizados com permissão e devem ser solicitados pelo site www.facit.org. Todos os questionários que compõem o *FACIT* foram submetidos a um desenvolvimento padronizado por um método válido que passou por cinco fases: (1) geração do item, (2) revisão e redução do item, (3) construção da escala, (4) avaliação inicial e (5) avaliação adicional para toda a medida do sistema (Cella e Mowinski, 2002).

O *FACT-G* foi desenvolvido e validado nos Estados Unidos para medir a qualidade de vida em pacientes adultos com câncer e está agora na versão 4 (Cella et al.,1993). Seus 27 itens contemplam quatro domínios: bem-estar físico, bem-estar social/familiar, bem-estar emocional e bem-estar funcional. Foi considerado apropriado para o uso em pacientes com qualquer tipo de câncer (Webster et al., 1999). O *FACT-G* foi concebido originalmente em inglês e submetido a processo de tradução para o português, o que incluiu duas traduções, uma tradução de reconciliação, uma retro-tradução da versão reconciliada e quatro revisões independentes por *expert* bilíngüe, tendo sido pré-testado em 19 pacientes com câncer em Portugal e em 30 pacientes no Brasil (Arnold et al., 2000; Arnold et al., 2001).

O *FACT-F* foi especialmente desenvolvido para medir a fadiga em pacientes com câncer. Consiste em um questionário que inclui o total de 40 itens, sendo 27 do *Functional Assessment of Cancer Therapy-General (FACT-G)*, para avaliação da qualidade de vida global, e 13 itens específicos sobre Fadiga (Yellen et al., 1997). A Subescala fadiga foi desenvolvida entre maio e outubro de 1994 e validada em

1997 em pacientes americanos. Avaliação da fadiga e qualidade de vida (QV) são importantes na avaliação comparativa de tratamentos, na tomada de decisões sobre futuros tratamentos, e em cuidados paliativos (Yellen et al.,1997). Este instrumento permite uma compreensão sobre o estado atual do paciente e a medição das mudanças ao longo do tempo, tornando-se uma ferramenta útil (Cella, 1997).

O questionário *FACT-F* tem sido utilizado para avaliar sintomas decorrentes de tratamentos de câncer, como a quimioterapia (Wadler et al., 2002; Downie et al., 2006) e a radioterapia (Wratten et al., 2004), a eficácia, dosagem e segurança de medicamentos para tratamento de anemia induzida pela quimioterapia (Vadhan-Raj, 2003; Gregory, 2006), nas intervenções com exercícios em pacientes com câncer e fadiga (Courneya et al., 2003; Segal et al., 2003; Dimeo et al., 2008), na terapia complementar em câncer (Tsang et al., 2007) e na intervenção de enfermagem (Godino et al, 2006).

A falta de um instrumento na língua desejada leva ao desenvolvimento de instrumentos no próprio idioma, ou utilização daqueles já existentes, após traduzi-los e validá-los (Prieto, 1992). Os instrumentos que foram desenvolvidos e validados em outros países devem ser validados e adaptados culturalmente no Brasil, devido a diferenças culturais existentes nessas populações.

O presente estudo refere sobre a validação do FACT-F na língua portuguesa e a escolha desse instrumento foi devido à sua comprovada aplicabilidade em vários estudos. No momento do início desta pesquisa não

havia instrumentos validados em português para mensurar fadiga no Brasil. Os questionários de fadiga atualmente validados no Brasil são o *Chalter Fatigue Questionnaire,* que foi validado em 2007 (Cho et al., 2007) e o *Piper Fatigue Scale,* validado recentemente em 2008 (Mota et al., 2008), e o crescente número de instrumentos validados reflete a importância desse assunto.

Após a validação do FACT-F, este instrumento foi utilizado para avaliar a fadiga e qualidade de vida em mulheres com câncer de mama antes da quimioterapia e depois do terceiro e sexto ciclos de quimioterapia.

O detalhamento do método referente a este estudo de validação e aplicação do FACT-F em mulheres com câncer de mama durante a quimioterapia está descrito no anexo 7.1, incluindo detalhes do cálculo do tamanho da amostra e os testes estatísticos utilizados.

2. Objetivos

2.1. Objetivo Geral

Validar a versão em português do questionário FACT-F em pacientes com câncer e avaliar a fadiga e a qualidade de vida em mulheres com câncer de mama em tratamento de quimioterapia.

2.2. Objetivos Específicos

- ***Artigo 1- Reproducibility of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) Questionnaire for Cancer Patients***

  Avaliar a reprodutibilidade do questionário *Functional Assessment of Cancer Therapy-Fatigue (FACT-F)* através do teste-reteste para a língua portuguesa em um período de 3 a 14 dias, em pacientes com câncer que se encontravam em tratamento de quimioterapia.

– ***Artigo 2- Validation of the Portuguese Version of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) in Brazilian Cancer Patients***

Validar para o português o questionário FACT-F, a fim de estabelecer propriedades incluindo a validade e confiabilidade em uma amostra de pacientes brasileiros com câncer.

– ***Artigo 3- Fatigue And Health-Related Quality of Life during 6 Cycles of Chemotherapy in Breast Cancer Patients***

Avaliar pacientes com câncer de mama antes do início da quimioterapia, e após 3º e 6º ciclos de quimioterapia, a fim de identificar mudanças na fadiga que poderão ocorrer após o início da quimioterapia; e determinar a relação entre a fadiga e a qualidade de vida relacionada à saúde controlada pela atividade física e tabagismo.

3. Publicações

Artigo 1 - ***Reproducibility of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) Questionnaire for Cancer Patients***

Artigo 2 - ***Validation of the Portuguese Version of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) in Brazilian Cancer Patients***

Artigo 3 - ***Fatigue and Health-Related Quality of Life During 6 Cycles of Chemotherapy in Breast Cancer Patients***

3.1. Artigo 1

Reproducibility of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) Questionnaire for Cancer Patients

Neli Muraki Ishikawa[1], Luiz Claudio Santos Thuler[2], Alessandra Grasso Giglio[1], Clarissa Seródio da Rocha Baldotto[1], Carlos José Coelho de Andrade[1], Sophie Françoise Mauricette Derchain[3]

[1] Brazilian National Cancer Institute (INCA), Rio de Janeiro.

[2] Rio de Janeiro State Federal University (UNIRIO) and Brazilian National Cancer Institute (INCA), Rio de Janeiro.

[3] State University of Campinas (UNICAMP), Campinas.

This study was done at National Institute of Cancer (Instituto Nacional de Câncer - INCA), Rio de Janeiro, RJ
Praça Cruz Vermelha, 23 - Centro
20230-130 - Rio de Janeiro - RJ

*Corresponding Author:
Neli Muraki Ishikawa
Serviço de Integração Humana, Instituto Nacional de Câncer (INCA) - Rua do Rezende, 128. CEP: 20231-092. Rio de Janeiro, RJ.
Tel: (21) 3970-7884 / 3970-7945
Email: nelimuraki@gmail.com

Artigo enviado em 24 de julho de 2008 para a revista *Applied Cancer Research*, conforme e-mail abaixo.

de	Sonia Calazans Pereira <sonia.pereira@appliedcr.org>
para	Neli Muraki Ishikawa <nelimuraki@gmail.com>
data	24 de julho de 2008 19:16
assunto	[ACR] Agradecimento pela Submissão
enviado por	hm415.locaweb.com.br

Neli Muraki Ishikawa,
Agradecemos a submissão do seu manuscrito "Reprodutibilidade do questionário de avaliação da fadiga FACT-F em pacientes com câncer" para Applied Cancer Research. Através da interface de administração do sistema, utilizado para a submissão, será possível acompanhar o progresso do documento dentro do processo editorial, bastanto logar no sistema localizado em:
URL do Manuscrito:
http://www.appliedcr.org.br/index.php/appliedcr/author/submission/135
Login: nelimuraki

Em caso de dúvidas, envie suas questões para este email. Agradecemos mais uma vez considerar nossa revista como meio de transmitir ao público seu trabalho.

Sonia Calazans Pereira
Applied Cancer Research
http://www.appliedcr.org

Artigo aceito em 28 de julho de 2008, conforme e-mail abaixo.

de	Erika Maria Monteiro Santos <erikammsantos@appliedcr.org>
para	Neli Muraki Ishikawa <nelimuraki@gmail.com>
data	28 de julho de 2008 12:28
assunto	Reproducibility of the questionnaire for assessing fatigue FACT-F in patients with cancer
enviado por	hm415.locaweb.com.br

Prezada Neli

Agradecemos a submissão do artigo Reproducibility of the questionnaire for assessing fatigue FACT-F in patients with cancer. O artigo foi revisto e aceito para publicação após as modificações sugeridas pelo revisor.
Solicito a realização destas sugestões no menor prazo possível e envio através do sistema de submissão. Os comentários do revisor estão abaixo.

Atenciosamente

Benedito Mauro Rossi
Editor-Chefe
Applied Cancer Research

Reviewer
1 - Relevância do artigo [moderada]
2 - Qualidade do título [boa]
3 – O resumo contempla os passos do planejamento do trabalho: objetivos, métodos, resultados e conclusão? [totalmente]
4 - Palavras-chave adequadas [sim]

INTRODUÇÃO
5 – A introdução tem qualidade e é pertinente [não]

6 - Corresponde ao tema proposto? [sim]
7 – Tamanho [nsuficiente]

OBJETIVO
8 - Apresentação adequada? [sim]

MÉTODOS
9 - O desenho do estudo (observacional transversal, coorte, caso-controle, experimental, metanálise) é apropriado? [sim]
10 A descrição dos critérios de exclusão e inclusão dos pacientes é adequada? [não]

RESULTADOS
11- Resultados apresentados correspondem às questões da pesquisa? [sim]
12 - Qualidade na apresentação dos resultados: [boa]
13 - Compreensão das tabelas, gráficos e figuras: [/boa/]

DISCUSSÃO
14 - A discussão é coerente com o desenvolvimento e com os resultados do trabalho? [parcialmente]

REFERÊNCIAS BIBLIOGRÁFICAS
15 – As referências são pertinentes [parcialmente]
16 - As referências são atualizadas [parcialmente]

O artigo aborda um tema relevante que é a reprodutibilidade dos questionários para avaliação da qualidade de vida.
A introdução é curta, e não aborda com clareza a importância de avaliar a fadiga. Também não contempla resultados obtidos com o FACT-F.
No método, a principal questão é que embora o artigo tenha se proposto a avaliar a reprodutibilidade, não há citação a avaliação da estrutura do artigo através da validade de constrututo.
Outro aspecto relevante é a forma de seleção dos pacientes que não ficou clara. Acredito que o serviço onde a pesquisa fora realizada tenha um grande fluxo de pacientes, no entanto a amostra se consituiu de 85 indivíduos. Os critérios de inclusão e a forma da seleção não ficou clara. Foram pacientes consecutivos que se apresentaram em um único dia de atendimento? Ou os pacientes foram sorteados? Qual o critério para a inclusão? Há cálculo no tamanho da amostra?
Também foi observado que parte da amostra respondeu o questionário e outra parte foi entrevistada. Foram observadas diferenças na reprodutibilidade entre os grupos de acordo com o método de administração? Há diferenças na reprodutibilidade de acordo com a escolaridade?

Applied Cancer Research
http://www.appliedcr.org

Prova do artigo 2 de dezembro de 2008, conforme e-mail abaixo.

de	Erika Maria Monteiro Santos <erikammsantos@appliedcr.org>
para	Neli Muraki Ishikawa <nelimuraki@gmail.com>
data	2 de dezembro de 2008 11:20
assunto	Re: [ACR] Proofreading Request (Author)
enviado por	appliedcr.org

Prezada Neli
Em anexo a segunda prova do artigo.

Atenciosamente
Erika Maria Monteiro Santos
Managing Editor
Applied Cancer Research

acr_135_reprodutibility prova 2.pdf 550K

Abstract

Objective: The objective of this study was evaluating the reproducibility in Portuguese of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) questionnaire for cancer patients by applying it according to the test-retest method. **Material and Methods:** Subjects were 85 cancer patients with an average age of 51.0 years, being 56 (65.9%) women and 29 (34.1%) men. FACT-F questionnaire consists of 40 items, divided in five domains, and is applied for evaluating quality of life and fatigue in patients with cancer. We used as a measuring tool intraclass correlation coefficient values obtained from two measures of test-retest and scatter plot proposed by Bland-Altman. **Results:** In 36.5% of cases the questionnaire was self-administered, and in 63.5% of the cases read by an interviewer and filled after verbal answer. Intraclass correlation coefficient values found for the domains were: physical well-being 0.72; social/family well-being 0.91; emotional well-being 0.90; functional well-being 0.86; fatigue subscale 0.88, and for the FACT-F 0.91. The Bland-Altman plot showed to be adequate, since most points were within the limits of reliability. **Conclusions:** FACT-F questionnaire in Portuguese has good test-retest reproducibility in patients with different types of cancer, performance status and stages.

Keywords: Quality of life; fatigue; questionnaire; reproducibility

Introduction

Fatigue is highly prevalent, affecting about 94% of patients with cancer. Its frequency increases significantly during chemotherapy and radiotherapy[1] and has a great impact on the quality of life of oncologic patients [1, 2].

Measuring fatigue has been widely used to evaluate the effects of treatments. It is also useful for studying new approaches and new ways of controlling symptoms, to improve the knowledge of doctors and to identify the necessities of the patients, aiming at the development of more adequate care strategies[3].

Cancer-related fatigue may be evaluated by specific one-dimensional or multidimensional instruments[1]. In a recent systematic review of the scientific literature, 14 fatigue-evaluating scales were found; the most common questionnaires were *Functional Assessment of Cancer Therapy Fatigue (FACT-F)*, *European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ C30) (fatigue subscale)* and it *Fatigue Questionnaire (FQ)* [4].

FACT-F questionnaire has been used to evaluate symptoms resulting from cancer treatments such as chemotherapy[5, 6] and radiotherapy[7], as well as the efficiency, dosage and security of medicines for chemotherapy-induced anemia [8, 9], in interventions involving exercises in patients with cancer and fatigue[10, 11, 12], in complementary cancer therapy [13], and in nursing interventions[14].

FACT-F consists of a questionnaire with a total of 40 items, being 27 items the *Functional Assessment of Cancer Therapy-General (FACT-G)*, for evaluating global quality of life, and 13 specific items related to Fatigue[15]. *FACT-F* is part of the measure system *Functional Assessment of Chronic Illness Therapy* (FACIT), which comprises a collection of health-related quality of life questionnaires. These

questionnaires were developed to be applied to patients with chronic diseases[16]. All FACIT questionnaires were submitted to a standardized development with valid methodology that passes through five phases: (1) generation of the item, (2) revision and reduction of the item, (3) construction of the scale, (4) initial evaluation and (5) additional evaluation for the whole system measure[17]. They are available in 45 languages, allowing the comparison of different populations, using a rigorous methodology of translation and back-translation, psychometric tests and cognitive interviews[16].

FACT-G specifically was developed and validated to measure the quality of life in adult patients with cancer and is now in its 4 version[18]. Its 27 items contemplate four domains: physical well-being, social/family well-being, emotional well-being and functional well-being. It is considered appropriate for patients with any type of cancer[19]. *FACT-G* was conceived originally in English and submitted to a translation process into Portuguese, which included two translations, a reconciliation translation, a back-translation of the reconciled version and four independent revisions by bilingual *expert*. It was pre-tested in 19 cancer patients in Portugal and 30 in Brazil [20,21]. However, the version in the Portuguese language was not validated for the Brazilian population. Thus, the use of FACT-F in Brazil requires to be validated and culturally adapted. The present study aims to evaluate the stability of version 4 of *FACT-F* questionnaire for the Portuguese language in its use with patients with cancer through the test –retest method[22].

Materials and Methods

Subjects selection

From September 2005 and February 2006, women and men with cancer treated with chemotherapy or hormone therapy in the outpatient department of Clinical Oncology of the Brazilian National Cancer Institute (INCA) were selected for the study. Patients were included with ages from 18 and 82 years and who were able to return to the Institution for consultations or treatment with other professionals, or to submit to examinations in a period from 3 to 14 days, which allowed the application of the retest. 85 patients were included in this study, a number higher than the minimum recommended sample size for test-retest reproducibility, which is at least 50 subjects[23, 24].

Subjects were excluded who had more than one cancer diagnosis, were pregnant at diagnosis, and with a diagnosed psychiatric disease. In the end, 85 patients were included. The present study was approved by the Committee of Ethics of Research of the Brazilian National Cancer Institute. All patients signed the Term of Free and Informed Consent before being included in the research.

Instruments

Functional Assessment of Cancer Therapy - Fatigue (FACT-F)

We used version 4 of *FACT-F,* with 40 items, including 27 of *FACT-G*, which evaluates specifically quality of life, and an additional domain with 13 specific items about Fatigue[15]. The use of the questionnaire was authorized and made available by the authors in Portuguese language for this research. The instrument explores, as said, five domains: physical well-being, social/family well-being,

emotional well-being and functional well-being and fatigue. The physical well-being domain has 7 items with scores from 0 to 28 points; social/family well-being, 7 items with score from 0 to 28 points; emotional well-being, 6 items with score from 0 to 24 points; functional well-being, 7 items with score from 0 to 28 points; and fatigue subscale, 13 items with score from 0 to 52. Each item has five *likert*-type options graduated from 0 to 4: “Not at all”, “A little bit”; “Somewhat”; “Quite a bit”; “Very much”. The final score of *FACT-F* is obtained by adding the scores of the five domains, and may vary from 0 to 160 points. The higher the number of points, the better the quality of life and the less the fatigue of the patients is. To obtain the score, the negative questions are reverted; then the answers of the domains are added up, and a proportional average is carried out in case of non answered items. It is acceptable a 50% score of non-answered questions. But 80% of answered questions are considered adequate[16]. The instrument make questions about health condition in the last seven days, and was written for a reading level of a fourth grader of elementary level (9 - 10 years of age), and it can be self administered, applied in the form of an interview, read by the researcher to the participants, and applied by telefone[16, 18].

Eastern Cooperative Oncology Group (ECOG) *Performance Status* (PS) [25]

For clinical evaluation of patients, we used the PS, a method of clinical evaluation of patients, recognized by the World Health Organization and widely used in patients with cancer. The scores vary from 0 to 4: PS 0 - normal activity; PS1 - symptoms of the disease, but ambulatory and with a normal daily routine; PS2 - out of bed more than 50 % of the time; PS3 - more than 50% of the time in bed, needing more intensive care; PS4 – restricted to bed.

Additional information

We also evaluated patient gender, marital status, and educational level, as well as the topography of the primary cancer, its stage and treatment. Demographic information on disease and treatment were obtained and collected from the medical register of patients.

Statistical analysis

Information obtained from the filled questionnaires was stored in an electronic environment, using Microsoft Excel and subsequently exported to the program *Statistical Package for the Social Sciences* (SPSS), version 13.0, for data consistency analysis and statistical treatment. Descriptive statistic (percentages or averages accompanied by the respective standard deviations) was calculated to describe the characteristics of the subjects and the scores of each domain of the *FACT-F*. The qui-square test was used for the analysis of the categorical variables. The reproducibility of the questionnaire was tested through two evaluations: one in the moment of the inclusion in the study and on second repeated after a period from 3 to 14 days (average 6.5 days ± 2.84), with the purpose to compare the results obtained by the same examiner in different times.

The reproducibility of information of the questionnaires was analyzed in the present study using two statistical procedures: intraclass correlation coefficient (ICC) for values obtained in two measurements (test-retest) and the scatter plot proposed by Bland-Altman, which compares graphically differences between values obtained in the test and the retest of FACT-F ($FACTF_{test}$ – $FACTF_{retest}$) with the averages of two evaluations [($FACTF_{test}$ + $FACTF_{retest}$)/2].

We considered as limit of agreement in Bland-Altman scatter plot twice the standard deviation of the average of the differences between the obtained results[26, 27]. Besides, we calculated Pearson correlation coefficient, aiming to compare results obtained with those of the original article of validation of FACT-F for the English language. Pearson correlation coefficient was classified in the following way: 0-0.25 - not correlated; 0.25-0.50 - weak correlation; 0.50-0.75 - moderated to good correlation; >0.75 very good to excellent correlation[28]. ICC can vary from 0 to +1, in this case indicating a high reproducibility, while ICC=0 indicates no reproducibility[29]. We used the significance level of a=0.05. We also calculated the confidence interval of 95 % (CI95%) for each ICC value.

Results

Sociodemographic and disease characteristics

Subjects of the study were 85 patients with an average age of 51.0 years (±12.2), varying from 19 to 82 years of age; 65.9% (n=56) were female and 34.1% (n=29) male; the marital status of this population was: 23.5% unmarried, 42.4% married, 17.6 % separated/ divorced and 16.5% widowers. Educational level was: 48.2% - elementary school; 35.3% -secondary school; 16.5% - college. As for the type of cancer, the most frequent were breast cancer (31.8%), colorectal cancer (21.4%), lymphoma (16.5%), lung (8.2 %), and other types (22.1%): stomach, myeloma, Ewing/PNET, soft tissue sarcoma, osteosarcoma, melanoma, bladder and tymoma. Most cases were stage IV (38.8%) followed by stage III (35.3%), stage II (24.7%) and stage I (1.2%), all being treated with chemotherapy; from these, 57.6% were submitted to surgery and 34.1% received radiotherapy.

Performance Status (PS) of subjects was: PS0 35.3%, PS1 51.8%, PS2 11.8%, PS3 1.2% and PS4 0%.

Administration of *FACT-F*

Regarding the way of administration the instrument, 36.5% self administered and 63.5% were interviewed by a researcher. Self-adminstration were carried out by patients younger than those interviewed (age average 47.42 versus 52.81; p = 0.048). Figure 1 compares the distribution of educational level and *performance status* according to the application of the questionnaire. Interviewed patients had less educational level (elementary and secondary school) (p <0,001). On the other hand, there was no statistically significant difference in *performance status* between the two different ways of applying the questionnaire (p=0.24).

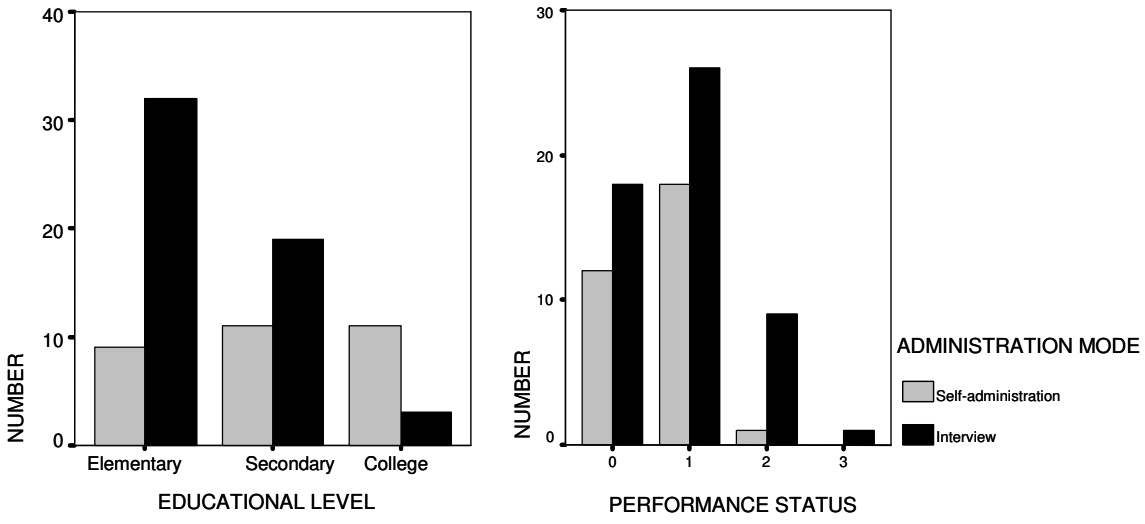


Figure 1 - Educational level and *performance status* of patients according to the *FACT-F* administration mode

Reproducibility

Table 1 shows the average, intraclass correlation coefficients and Pearson correlation of scores obtained in the different domains regarding the test and the retest. No significant differences were observed on averages between the domains for the first and the second interviews. Values found for ICC for the domains varied between 0.72 for physical well-being and 0.91 for social/family well-being; fatigue subscale reached 0.88 and FACT-F as a whole, 0.91. Pearson correlation coefficient was excellent (r> 0.75) for all domains, except for well-being physical, that presented a moderated correlation (r = 0.58). The highest correlation found referred to social/family well-being (r = 0.84). The correlation coefficient was excellent for *FACT-F* (r =0.85). These high correlation coefficients indicate a high degree of stability in time, showing that there were no significant changes in measures of quality of life and fatigue.

Table 1 - Average, intraclass correlation coefficient and Pearson correlation coefficients of scores of the different domains in test and retest (n=85)

Domains (scores variation)	**Average (± SD)**		**Intraclass correlation (CI95%)**	**Pearson Correlation**
	Test	**Retest**		
Physical Well-Being (0-28)	22.70 (± 3.93)	21.69 (± 4.54)	0.72* (0.58-0.82)	0.58*
Social/Family Well-Being (0-28)	21.71 (± 4.12)	21,00 (± 4.33)	0.91* (0,86-0.94)	0.84*
Emotional Well-Being (0-24)	20.00 (± 4.42)	19.88 (± 4.09)	0.90* (0.86-0.94)	0.83*
Functional Well-Being (0-28)	18.94 (± 5.17)	17.99 (± 5.36)	0.86* (0.79-0.91)	0.76*
Subscale Fatigue (0-52)	41.43 (± 7.79)	41.26 (± 9.18)	0.88* (0.81-0.92)	0.79*
FACT-F (0-160)	124.79 (± 19.20)	121.01 (± 22.10)	0.91* (0.86-0.94)	0.85*

FACT-F: Functional Assessment of Cancer Therapy Fatigue; SD: standard deviation; CI: confidence interval. * *p* value <0.0001.

Intraclass correlation did not vary regarding educational levels for the physical well-being domain (elementary school: ICC=0.79, CI 95% = 0.61-0.89; secondary: ICC=0.64. CI 95% = 0.25-0.82; college: ICC=0.58. CI 95% =0.35-0.87); social/family well-being (elementary school: ICC=0.96. CI 95% = 0.94-0.98; secondary school: ICC=0.81. CI 95% = 0.59-0.91; college: ICC=0.57. CI 95% =0.27-0.86); emotional well-being (elementary school: ICC=0.94. CI 95% = 0.89-0.97; secondary school: ICC=0.86. CI 95% = 0.71-0.93; college: ICC=0.75. CI 95% = 0.24-0.92); functional well-being (elementary school: ICC=0.89. CI 95% = 0.81-0.94; secondary school: ICC=0.76. CI 95% = 0.49-0.89; college: ICC=0.79 CI 95% = 0.36-0.93); subscale fatigue (elementary school: ICC=0.93. CI 95% = 0.87-0.96; secondary school: ICC=0.79, CI 95% = 0.57-0.90; college: ICC=0.65. CI 95% =0.12-0.893) and for FACT-F (elementary school: ICC=0.94. CI 95% = 0.88-0.97; elementary school: ICC=0.80, CI 95% = 0.57-0.91; college: ICC=0.79, CI 95% = 0.40-0.93).

As for the way of applying the questionnaire, there was no intraclass correlation difference between domains: physical well-being (interviewed: ICC=0.83, CI 95% = 0.49-0.83; self-administered: ICC=0.69, CI 95% = 0.36-0.85); social/family well-being (interviewed: ICC=0.92, CI 95% = 0.87-0.96; self-applied: ICC=0.88, CI 95% = 0.62-0.95); emotional well-being (interviewed: ICC=0.89, CI 95% = 0.81-0.93; self-applied: ICC=0.93, CI 95% = 0.85-0.96); functional well-being (interviewed: ICC=0.87, CI 95% = 0.78-0.93; self-applied: ICC=0.83, CI 95% = 0.59-0.92); fatigue subscale (interviewed: ICC=0.91, CI 95% = 0.84-0.95; self-applied: ICC=0.82, CI 95% = 0.63-0.91) nor for FACT-F (interviewed: ICC=0.93, CI 95% = 0.88-0.96; self-applied: ICC=0.87, CI 95% = 0.61-0.94).

Figure 2 presents Bland-Altman dispersal diagram showing the average values of FACT-F scores (abscissa) and the individual differences between values obtained in the test and in the retest (ordinate). The average of differences found was 3.78 (standard deviation= 11.70) and the limits (average ± 2 standard deviations) were +27.18 and -19.62. Most points are contained on the established limits. An analysis of the difference between the averages of test and retest reveals the distribution of the points to be concentrated near to average value of the differences, and only two cases were higher than the superior limit and one less than the inferior limit, thus confirming the good agreement between test and retest.

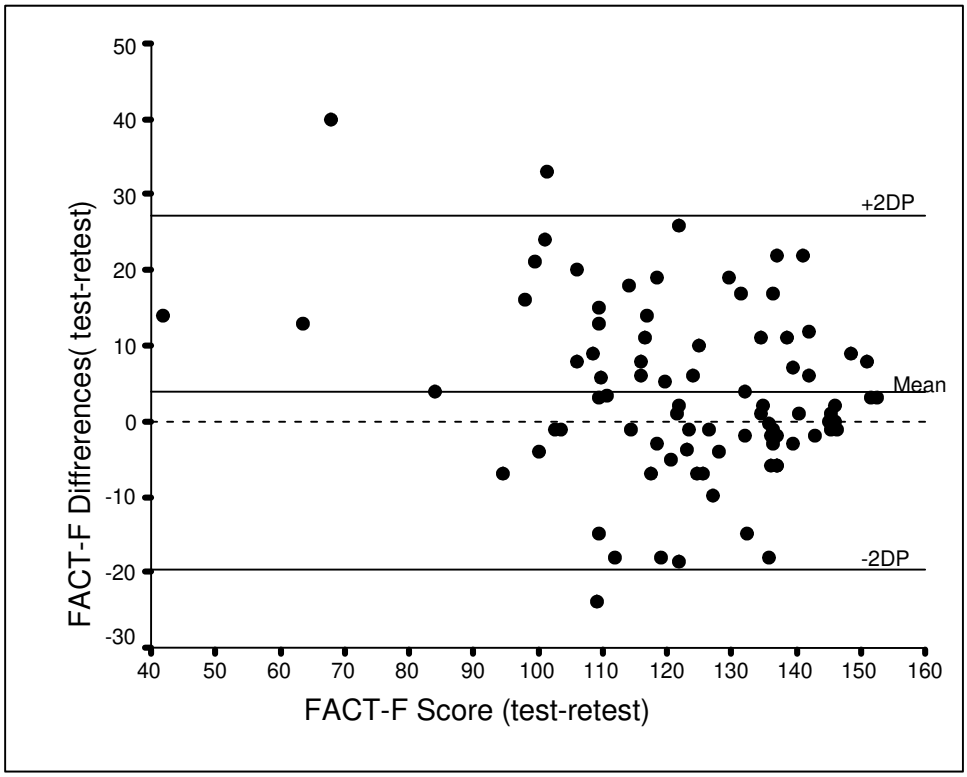


Figure 2. Bland-Altman scatter plot for agreement between the test and retest of the application of FACT-F questionnaire for the evaluation of fatigue and quality of life in patients with cancer

Discussion

Several instruments for evaluating quality of life in patients with cancer are being developed in Europe and the United States mainly in the English language[30, 31]. Using such an instrument in Brazil requires a trans-cultural adaptation by using psychometric measures [32, 33]. One of the stages for validating a questionnaire is the test - retest of the version translated to Portuguese. In this study the instrument *FACT-F* was applied to 85 patients with different types of cancer. The participants of this research had mainly cancer in stages III and IV, the profile of the population treated in INCA, where more than 50% of the patients present advanced disease at diagnostic[34].

Sixty three per cent of the individuals had chosen the interview; in it the questionnaire was read and filled out by the interviewer, instead of self administered. This can be due to the low educational levels and to the fact that most patients are aged. The same happened in the study for validation of *FACT-G* in Spanish for patients with cancer in Uruguay[35].

We noticed no significant differences between the averages of the scores of four analyzed domains of *FACT-G* and the fatigue subscale. Intraclass correlation did not differ regarding educational levels and way of application.

Intraclass correlation coefficient was high for all domains, and the highest intraclass correlation was obtained for the social/family well-being domain (ICC=0.91) and the FACT-F questionnaire that obtained an excellent ICC (ICC=0.91). The lowest correlation was observed in the physical well-being domain (ICC=0.72). As in the study of Yellen et al.[15] intraclass correlation was not calculated, a comparison is not possible with the present study. We also observed that Bland-Altman scatter

plot showed a small difference between the scores of the test and the retest, because most points were inside the established limits.

Pearson correlation coefficients values found in the present study for FACT-F (r=0.85) and the subscale fatigue (r=0.79) are lightly inferior to the values of Pearson correlation coefficients observed for FACT-F (r=0.87) and the subscale fatigue (r=0.90) in the validation study of the original FACT-F English version questionnaire, published by Yellen et al.[15], which applied it to 50 subjects from 19 to 83 years of age, with test - retest in an interval from 3 to 7 days. In the present study it was not possible to determine if this difference was due to instability of the clinical condition of patients, since some retests were carried out up to 14 days after test, when their condition might be equal, worse or better that in the day of test.

Although in the present study we used Pearson correlation coefficient, mainly for comparing results obtained to those of already published studies, it is known that it has limitations as a tool for evaluating agreement, for it evaluates only linear relations between the variables and do not account for a systematic bias[26, 27,] something that makes ICC preferable for evaluate reproducibility.

Besides, since in the second application the patient already knows the instrument, reproducibility may be overestimated; conversely, the variations in the health condition and in learning may underestimate it. In spite of these limits, the analysis of reproducibility is important for the evaluation of the instrument's stability [22].

Conclusion

This study demonstrated that the *FACT-F* instrument has a good reproducibility test - retest in heterogeneous series of patients, with different types of cancer,

performance status and staging, what allows it to be applied in Brazilian studies on quality of life and fatigue in patients with cancer, making possible to compare the results of evaluations and interventions with other studies carried out in the country.

Conflicts of Interest: None

Acknowledgements

The authors thank Dr. Ben Arnold and Dr. Helen Morrow for permitting the use of the FACT-F instrument in this study and making available its Portuguese language version. We also thank Sirlei Siani Morais for reviewing the statistic analysis.

Collaborators

N M Ishikawa contributed in the preparation of the manuscript of the study, data collection, editorial assistance, statistic analysis, discussion of results and final approval of the text. L C S Thuler contributed to the review of the content of the paper, statistic analysis, discussion of results and final approval of the text. AG Giglio contributed for the choice of patients, data collection and has also taken part in the final approval of the text. C S R Baldotto contributed for the choice of patients, data collection and has also taken part in the final approval of the text. C J C Andrade contributed for the choice patients, data collection and has also taken part in the final approval of the text. S F M Derchain was responsible for conceiving and designing the study, has taken part of the review of the content of the paper and the final approval of the text.

References

1. Ishikawa NM, Derchain SFM; Thuler LCS. Fadiga em pacientes com câncer de mama em tratamento adjuvante. Rev Bras Cancerol. 2005; 51(4):313-318.

2. Curt GA. Impact of fatigue on quality of life in oncology patients. Semin Hematol. 2000; 37 Suppl 6:14-7.

3. Flechtner H, Bottomley A. Fatigue and quality of life: lessons from the real world. The Oncologist. 2003; 8: Suppl 1, 5–9.

4. Minton O, Stone P. A systematic review of the scales used for the measurement of cancer-related fatigue (CRF). Ann Oncol. Annals of Oncology Advance Access published August 4, 2008, doi:10.1093/annonc/mdn537.

5. Downie FP, Mar Fan HG, Houédé-Tchen N, Yi Q, Tannock IF. Cognitive function, fatigue, and menopausal symptoms in breast cancer patients receiving adjuvant chemotherapy: evaluation with patient interview after formal assessment. Psychooncology. 2006; 15(10):921-30.

6. Wadler S, Brain C, Catalano P, Einzig AI, Cella D, Benson AB 3rd. Randomized phase II trial of either fluorouracil, parenteral hydroxyurea, interferon-alpha-2a, and filgrastim or doxorubicin/docetaxel in patients with advanced gastric cancer with quality-of-life assessment: eastern cooperative oncology group study E6296. Cancer J. 2002; 8(3): 282-6.

7. Wratten C, Kilmurray J, Nash S, Seldon M, Hamilton CS, O'Brien PC, Denham JW. Fatigue during breast radiotherapy and its relationship to biological factors. Int J Radiat Oncol Biol Phys. 2004; 59(1):160-7.

8. Gregory SA. Efficacy of darbepoetin alfa in the treatment of chemotherapy-Induced anemia in non-hodgkin's lymphoma. Support Cancer Ther. 2006; 3(4):232-9.

9. Vadhan-Raj S, Mirtsching B, Charu V, Terry D, Rossi G, Tomita D, McGuire WP. Assessment of hematologic effects and fatigue in cancer patients with chemotherapy-induced anemia given darbepoetin alfa every two weeks. J.Support Oncol. 2003; 1(2):131-8.

10. Dimeo F, Schwartz S, Wesel N, Voigt A, Thiel E. Effects of an endurance and resistance exercise program on persistent cancer-related fatigue after treatment. Ann Oncol. 2008; 19(8):1495-9.

11. Segal RJ, Reid RD, Courneya KS, Malone SC, Parliament MB, Scott CG, et al. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. J Clin Oncol. 2003*;* 21(9):1653-9.

12. Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes. J Clin Oncol. 2003; 21:1660-8.

13. Tsang KL, Carlson LE, Olson K. Pilot crossover trial of Reiki versus rest for treating cancer-related fatigue. Integr Cancer Ther. 2007; 6(1):25-35.

14. Godino C, Jodar L, Durán A, Martínez I, Schiaffino A. Nursing education as an intervention to decrease fatigue perception in oncology patients. Eur J Oncol Nurs. 2006; 10(2):150-5.

15. Yellen SB, Cella DF, Webster K, Blendowski C, Kaplan E. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. J Pain Symptom Manage. 1997;13(2):63-74.

16. Webster K, Cella D, Yost K. The functional assessment of chronic illness therapy measurement system: properties, applications, and interpretation. Health and Quality of Life Outcomes. 2003; 1:79.

17. Cella D; Mowinski CJ. Measuring quality of life in chronic illness: the funtional assessment of chronic illness therapy measurement system. Arch Phys Med Rehabil. 2002; 83(suppl 2):s10-s17.

18. Cella D, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, et al. The functional assessment of cancer therapy scale: development and validation of the general measure. J Clin Oncol. 1993; 11: 570-79.

19. Webster K, Odom L, Peterman A, Lent L, Cella D. The functional assessment of chronic illness therapy (FACIT) measurement system: validation of version 4 of the core questionnaire. Qual Life Res. 1998; (7), 604.

20. Arnold BJ, Eremenco E, Chang CH, Odom L, Ribaudo JM, Cella D. Development of a single portuguese language version of the functional assessment of cancer therapy general (FACT G) scale. Qual Life Res. 2000; 9(3): 316.

21. Arnold BJ, Eremenco E, Chang CH, Cella DF, Ribeiro JLP, Doro MP, *et al.* How much is “very much”? Developing a rating scale for portuguese speaking countries. Qual Life Res. 2001; 10(3): 264.

22. Scientific Advisory Committee of the Medical Outcomes Trust (Aaronson N, Alonso J, Burnam A, Lohr KN, Patrick DL, Perrin E, Stein REK). Assessing health status and quality-of-life instruments: attributes and review criteria. Qual Life Res. 2002; 11: 193-205.

23. Hopkins WG. Measures of reliability in sports medicine and science. Sports Med. 2000; 30(1):1-15.

24. Atkinson G, Nevill A. Typical error versus limits of agreement. Sports Med. 2000; 30(5):375-81.

25. Zubrod CG, Schneiderman M, Frei E. Appraisal of methods in the study of chemotherapy in man: comparative therapeutic trial mustard and Triethylene thiophosphoramide. J. Chron Dis. 1960; 11:7-13.

26. Bland JM, Altman DG. Measurement in medicine: the analysis of method comparison studies. Statistician. 1983; 32:307-17.

27. Bland, J. M. Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986; 8476(1):307-10.

28. Colton T. 1974 Statistics in Medicine (p 211) Boston: Little, Brown and Company.

29. Szklo M, Nieto FJ. Epidemiology: Beyond the Basics (p 495) Maryland: Aspen Publishers.

30. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36) I: conceptual framework and item selection. *Med Care*. 1992; 30(6):473-83.

31. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ. The European Organization for Research and Treatment of Cancer QLQ-30: a

quality of life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993; 85: 365-75.

32. Fleck MPA, Louzada S; Xavier M, Chachamovich E, Vieira G, Santos L, Pinon V. Aplicação da versão em português do instrumento de avaliação de qualidade de vida da Organização Mundial da Saúde (WHOQOL-100). *Rev Saúde Pública*.1999; 33(2):198-205.

33. Ciconelli RM, Ferraz BF, Santos W, Meinão I, Quaresma MR. Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida. Rev Bras Reumatol. 1999; 39 (3):143-50.

34. BRASIL. Ministério da Saúde. Instituto Nacional de Câncer. Registro Hospitalar de Câncer: dados dos hospitais do INCA, relatório anual 1994/1998. Rio de Janeiro; 2004.

35. Dapueto JJ, Francolino C, Servente L, Chang CH, Gotta I, Levin R, et al. Evaluation of the Functional Assessment of Cancer Therapy-General (FACT-G) spanish version 4 in South America: classic psychometric and item response theory analyses. Health and Quality of Life Outcomes. 2003; 1:32.

3.2. Artigo2

Validation of the Portuguese Version of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) in Brazilian Cancer Patients

Neli Muraki Ishikawa, Luiz Claudio Santos Thuler, Alessandra Grasso Giglio, Clarissa Seródio da Rocha Baldotto, Carlos José Coelho de Andrade, Sophie Françoise Mauricette Derchain

Neli Muraki Ishikawa
Address for correspondence: Brazilian National Cancer Institute - INCA, Physical Therapy Department. Rua do Rezende, 128. Centro - Rio de Janeiro, RJ. Brasil CEP 20231-092. e-mail: nelimuraki@gmail.com

Luiz Claudio Santos Thuler
Federal University of the State of Rio de Janeiro - UNIRIO. Rua Mariz e Barros, 775. Maracanã - Rio de Janeiro, RJ. Brasil CEP 20270-004
e-mail: lthuler@gmail.com

Alessandra Grasso Giglio
Brazilian National Cancer Institute - INCA - Hospital of Cancer II, Rua Equador, 831 - Santo Cristo - Rio de Janeiro, RJ. Brasil CEP 20220-410
e-mail: laxgiglio@bol.com.br

Clarissa Seródio da Rocha Baldotto
Brazilian National Cancer Institute – INCA, Clinical Oncology Department, Praça da Cruz Vermelha, nº23. Centro - Rio de Janeiro, RJ. Brasil CEP 20230-130
e-mail: cbaldotto@gmail.com

Carlos José Coelho de Andrade
Brazilian National Cancer Institute - INCA, Clinical Oncology Department, Praça da Cruz Vermelha, nº23. Centro - Rio de Janeiro, RJ. Brasil CEP 20230-130
e-mail: carlosj@inca.gov.br

Sophie Françoise Mauricette Derchain
Campinas State University, Department of Obstetrics and Gynecology. Rua Antônio Hossri, 629 Cidade Universitária, Campinas, São Paulo, Brazil CEP13083-370
e-mail: derchain@fcm.unicamp.br

Artigo enviado em 23 de setembro de 2008 para a revista Supportive Care in Cancer.

de	Editorial Office <aschiess@sg.zetup.ch>
para	nelimuraki@gmail.com
data	23 de setembro de 2008 13:19
assunto	JSCC: Submission Confirmation for Validation of the Portuguese Version of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) in Brazilian Cancer Patients
enviado por	editorialmanager.com

Dear Mrs Ishikawa,

Your submission entitled "Validation of the Portuguese Version of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) in Brazilian Cancer Patients" has been received by journal Supportive Care in Cancer

You will be able to check on the progress of your paper by logging on to Editorial Manager as an author. The URL is http://jscc.edmgr.com/.

Your manuscript will be given a reference number once an Editor has been assigned.

Thank you for submitting your work to this journal.

Kind regards,

Editorial Office
Supportive Care in Cancer

Abstract

Goals of work: The purpose of this study was to validate the Portuguese version of the Functional Assessment of Cancer Therapy – Fatigue in order to establish properties including validity and reliability in a sample of Brazilian cancer patients.

Materials and methods: 270 patients with different types of cancer were included for this study; the mean age was 50.5 years. The reliability was assessed by internal consistency and reproducibility. Convergent validity was examined by comparing the FACT-F to the SF-36. Discriminant validity of the FACT-F evaluated the ability of the scale to differentiate defined group discriminating patients according at ECOG Performance Status, and different stages of disease.

Main results: FACT-F had high internal consistency (Cronbach a coefficient was 0.78 for physical well-being, 0.68 for social/family well-being, 0.75 for emotional well-being, 0.74 for functional well-being, 0.91 for fatigue, and 0.92 for total FACT-F). The range of test-retest intraclass correlation was from 0.72 to 0.91 ($p<0.0001$). The Pearson product correlation revealed good correlations between the total FACT-F and subscales of the SF-36 in most dimensions, ranging from $r=0.51$ to $r=0.76$, except to SF- 36 physical ($r=0.31$). Theses correlations were highly significant ($p<0.001$). The significant positive correlation between the FACT-F total ($r=0.76$), fatigue subscale ($r=0.77$), and SF-36 vitality scale support the convergent validity.

Conclusions: The Portuguese version of FACT-F is a reliable and valid instrument to assess QOL and fatigue, representing a valid tool to screen cancer-related fatigue in Brazilian cancer patients.

Key words: fatigue, quality of life, *FACT-F*, questionnaire, cancer

Introduction

Fatigue is one the most frequently reported symptoms accompanying cancer and its treatment [1]. Fatigue occurs between 1% and 94% in patients with cancer, with frequency increasing significantly during chemotherapy and radiotherapy [2]. Fatigue during cancer therapy can also have significant adverse effects on a patient's quality of life through its effects on anxiety and depression [3, 4], pain [5, 6], sleep quality [7], and ability to carry on daily activities [6]. Cancer-related fatigue not only interferes with daily activity, but also has a great impact on quality of life [8].

At a research level, the assessment of fatigue is clearly necessary to evaluate treatments. It is also necessary for the design of new approaches and new ways to monitor the effectiveness of interventions, for the improvement of clinicians' knowledge and awareness of patients' needs, and for the development of appropriate strategies for individual patient care [9].

The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System, under development since 1987, produced its 4th version in November 1997 [10]. The FACIT system [11] includes the Functional Assessment of Cancer Therapy (FACT), the Functional Assessment of Human Immunodeficiency Virus Infection (FAHI), and the Functional Assessment of Multiple Sclerosis (FAMS). The FACT scale is a well-documented scale for measurements of quality of life (QOL) among cancer patients. The FACT-G (General) scale [12] in combination with the "additional concerns" subscale provides a disease-specific quality of life assessment for various cancers like

prostate (FACT-P) [13], colorectal (FACT-C) [14], brain (FACT-Br) [15], lung (FACT-L) [16], and etc. These questionnaires were developed in North America, and many have been translated into almost 45 languages. One of the strengths of this ongoing translation project is its use of input from patients, linguists, psychologists and physicians internationally to assure that the wording of Version 4 is more cross-culturally relevant and more sensitive to measuring the psychosocial impact of illness in cultures outside the United States [11].

FACT-F [17] was especially developed to measure fatigue in cancer populations. The FACT-F (version 4) is a 40 item compilation, subdivided into four primary QOL domains and a disease-specific, domain-additional concern (fatigue). Accurate assessment of QOL, including the component expressed as fatigue or influenced by fatigue, is important when evaluating comparative treatments, making decisions about future treatments, and in palliative care [17]. The value of accurate QOL assessment is twofold: (a) it allows for an immediate understanding of an individual patient's current status (making it a potentially useful intervention tool); and (b) it allows for measurement of change over time, making it a useful outcome tool [18]. Subscale was developed between May 1994 and October 1994 and validated in 1997 with American patients. Development of the subscale occurred in two phases: item development (which included item generation, followed by item reduction and subscale validation).

The FACIT translation methodological attempts to attain the five dimensions of equivalence, namely, semantic/linguistic, content, conceptual, criterion, and technical dimensions, in cross-cultural translation [19].

The FACT-G was originally designed in English and was submitted to a Portuguese translation, which included two forward translations, one reconciled version, a back-translation of the reconciled version, and four independent reviews by bilingual experts. There was an equal representation from Brazil and Portugal, with one forward translator and two reviewers from each country. Only one Portuguese language version was developed for use in both Brazil and Portugal [20, 21]. Meanwhile this version has not been validated for the Brazilian population.

The purpose of this study was to validate the Portuguese version of the FACT-F and establish properties including validity and reliability in a sample of Brazilian cancer patients.

Patients and methods

276 patients were selected for this study, six patients refused to participate; reasons for that include lack of time or feeling of illness, the final sample validation sample consisted of 270 participants. The validity of FACT-F was established by evaluating the convergent and discriminant validities. The convergent validity was examined by comparing the FACT-F to the MOS 36-Item Short-Form Health Survey SF-36 [22, 23]; both instruments measures the health-related QOL. The SF-36 is a known valid and reliable QOL instrument and was validated in Brazil [24]. Discriminant validity of the FACT-F evaluated the ability of the scale to differentiate defined group discriminating patients according at ECOG Performance Status, and different stages of disease. The reliability was assessed by internal consistency and reproducibility.

Participants/Subjects

Study patients were selected from the Oncology Department of the Brazilian National Cancer Institute (INCA). Data was collected between September 2005 and June 2006. The inclusion criteria were to be 18 years of age or older and to be in cancer treatment with chemotherapy or hormone therapy. Exclusion criteria included: pregnancy; subjects with more than one diagnosis of cancer; and patients with a psychiatric diagnosis.

This study was approved by the Research Ethics Committee of the Brazilian National Cancer Institute; participation was voluntary and a written informed consent was obtained before completion of the instruments. Eligible oncology patients were asked to participate in a interview designed to elicit a variety of information using a structured interview format pertinent to sociodemographic information. The disease and treatment information was also collected from the patient's medical file. The mode of administration of the FACT-F (self-administration vs. read in interview) was registered in 270 cases.

Instruments

The validation packet of questionnaires administered to all participants included the FACT-F [17], MOS 36-Item Short-Form Health Survey (SF-36) [22, 23], Eastern Cooperative Oncology Group (ECOG) Performance Status Rating [25].

FACT-F [17, 18], version 4 consists of a 40 item self-report instrument that includes 40 likert-type items in 4 scale that assess a quality of life across the domains of physical well-being (seven items), which is the patient's actual

physical experience of a disease and/or treatment, including disease symptoms and treatment side effects; social/family well-being (seven items), which encompasses activities with and support from family and friends; emotional well-being (six items), which refers not only to emotional distress, but also to positive well-being or life happiness; and functional well-being (seven items), which refers to a person's ability to engage in the usual basic activities of daily living; and one scale with 13 item fatigue that assess fatigue. Subjects were asked to respond to each item with a score from 0 to 4, where 0= not all, 1= a little bit, 2= somewhat, 3= quite a bit, and 4= very much. The possible range of scores is from 0 to 160. A higher score indicates a higher level of QOL and lower level of fatigue.

MOS 36-Item Short-Form Health Survey (SF-36) [22, 23]: consists of 36 questions designed to measure health status and QOL domains, designed for use in clinical practice and research, health policy evaluations, and general population surveys. Eight health-related concepts are included in this instrument and are as follows: physical functioning (limitations in physical activities because of health problems); social functioning (limitations in social activities because of physical or emotional problems); role limitations due to physical functioning (limitations in usual role activities because of physical health problems); body pain; general health perceptions; vitality (energy and fatigue); role limitations caused by emotional problems; and mental health (psychological distress and well-being). The SF36 vitality scale is a four item measure which asks the respondent to indicate on a six-point frequency scale (1= all of the time and 6=none of the time) the extent to which the person feels full of energy versus

feeling tired and worn out during the previous 4 weeks. Scores are calculated and transformed to a 0 to 100 scale, with higher scores indicating increased health status.

Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) [25] is a five-point scale ranging scores from 0 (fully ambulatory without physical symptoms), 1 (fully ambulatory with some symptoms), 2 (requiring <50% awake time to rest), 3 (requiring >50% awake time to rest), to 4 (bedridden). It is widely used in cancer patient trials to assess functional capability of patients as they undergo treatment. It is used as an independent prognostic predictor in patients with cancer. The ECOG PS item was included because it is a familiar, somewhat global index.

Questionnaire for Demographic and Disease Information, a demographic information sheet that covers basic patient information such as age, sex, educational level, and marital status. A disease sheet covers a patient's diagnosis, treatment status and clinical stage.

Statistical Methods/Analysis

Reliability: The internal consistency of FACT-F was evaluated by calculating the Cronbach a coefficients for both the sub scores and for the total scores of the instruments [26]. The Cronbach a coefficient ranges from 0 to 1, the acceptable Cronbach coefficient was set at approximately 0.70 in accordance with the recommendations of Nunnally and Berenstein [27]. The coefficients obtained in our population were compared with those obtained by Yellen in another cancer population [17]. Reproducibility (test-retest) assesses

stability of the instrument over time. This was assessed by intraclass correlation coefficients (ICC) between the first and the second assessment for the same patient.

Validity: Validity was assessed by comparing the subscale scores and total scores of FACT-F with those of the SF-36, and using Pearson product moment correlation coefficient, and SF-36 vitality subscale comparing FACT-F fatigue subscale. It was expected that there would be a relatively high correlation between the FACT-F, fatigue subscale, and SF-36 vitality subscale.

Discriminant (known- groups) validity of the FACT-F was evaluating the ability of the scale to differentiate defined group discriminating patients according to ECOG PS, and different stages of disease. All subscales and total FACT-F sample were divided into three levels (PS=0, 1, and = 2), due to the small number, patients rated "3" or "4" on ECOG PS were combined with individuals rated "=2". Scheffé post-hoc comparisons were tested to show differences in FACT-F total and subscale scores according to ECOG PS and stage of illness. It was expected that better performance status and stage I would be associated with higher QOL. All analyses were performed using *Statistical Package for the Social Sciences* (SPSS) 13.0.. For all tests, a significance level of 0.05 was chosen, and all *p* were two-tailed.

Results

Demographic and Clinical Characteristics of the Participants

Six patients refused to participate; reasons for that include lack of time or feeling of illness. The validation sample consisted of 270 participants, of whom

201(74.4%) were women and 146 (54.1%) were married. The mean age of the patients was 50.5 years, with a range of 19-82 years; 141 (52.2%) were white, 164 (60.7%) had attended = 8 year of educational level. Patients represented a broad spectrum of disease, and the majority had diagnosed breast cancer (50%); had stage III (37.0%) and had performance status 1 (54.8%). All patients were currently undergoing chemotherapy and 32.2 % were in radiotherapy. Demographic and clinical information is available in Table 1.

Although the FACT-F was designed for self-administration, most patients (N=211, 78.1%) in our sample were interviewed due to low educational level.

Reliability

Internal consistency was evaluated by calculating the Cronbach a coefficient, which was 0.78 for physical well-being, 0.68 for social/family well-being, 0.75 for emotional well-being, 0.74 for functional well-being, 0.91 for fatigue, and 0.92 for total FACT-F, indicating satisfactory internal consistency. Table 2 shows alpha coefficient and mean of FACT-G for the Brazilian Portuguese version.

Test-retest reliability involved administration of 85 retest administration of the FACT-F within 3-14 days. The test-retest [28] was assessed by intraclass correlation (ICC) between the first and the second assessments for the same patient, the coefficients were 0.72 (95% CI=0.58-0.82) for physical well-being, 0.91 (0.86-0.94) for social/family well-being, 0.90 (0.86-0.94) for emotional well-being, 0.86 (0.79-0.91) for functional well-being, 0.90 (0.81-0.92) for fatigue, and 0.91 (0.86-0.94) for total FACT-F.

Validity

The Pearson product correlation revealed good correlations between the total FACT-F and subscales of the SF-36 in most dimensions (Table 3)., ranging from $r = 0.51$ to $r = 0.76$, except for SF- 36 physical ($r = 0.31$). As expected, the significant positive correlation between the FACT-F total ($r = 0.76$), fatigue subscale ($r = 0.77$), and SF-36 vitality scale support the convergent validity, confirming that they are measuring the same domain, fatigue. Intercorrelations among subscales and the total scores of fatigue, means, and standard deviations appear in Table 3. Pearson correlation coefficients were high between the FACT-F total score and its subscale scores, ranging from $r = 0.50$ to $r = 0.88$.

Discriminant validity was examined by ECOC PS and stage of illness in relation to the subscales and total FACT-F. It was shown in Table 4 that the subjects who scored higher on the FACT-F had a better PS. Scheffé post-hoc comparisons suggested that physical, functional, fatigue subscale and total FACT-F were able do discriminate between PS=0 versus 1, =2 and PS=1 versus =2 ($p < 0.001$), social/family well-being was able to discriminate PS=0 versus =2 ($p < 0.018$), and emotional well-being was able to discriminate PS=0, 1 versus =2 ($p < 0.001$). Scheffé post-hoc comparisons suggested that physical, emotional, functional, fatigue subscale, and total FACT-F were able to discriminate between stage of disease = I, II, III versus IV, ($p < 0.001$) reflecting a poorer QOL, but not in social/family well-being where the scores wasn't significant to differentiate between stage differences ($p = 0.470$) (Table 4).

Discussion

FACT-F [17, 18] was designed to provide information about fatigue and quality of life. The FACT-F was translated also into Japanese and the psychometric properties have been established [29].

The purpose of this study was to validate the Portuguese version of the FACT-F for use with Brazilian cancer patients. In the previous study [28] it was assessed the FACT-F reproducibility in 85 Brazilian cancer patients and 36,5% of the cases the questionnaire was self administered, and in 63.5% of the cases they had been read by interviewer and filled after verbal answer. *FACT*-F questionnaire in Portuguese language has good test-retest reproducibility in patients with different types of cancer, performance status and stages.

The internal consistencies of FACT-F and fatigue subscale were highly satisfactory. With the exception of reduced social and family well-being, the results indicated good reliability. The lower Cronbach coefficient noted for social and family well-being is consistent with a previous study [12]. The findings in the internal consistency of FACT-F and fatigue subscale respectively in Brazilian (0.91, 0.92), American (0.93, 0.95) [17], and Japanese (0.93, not avalilable) [29] samples are very similar. The results show little differences and might reflect cultural differences and not a true difference in fatigue experience. Another explanation is based on the difference in disease presentation between the samples. Half of the Brazilian sample consists of women with breast cancer, whereas a quarter of the American sample, and the Japanese sample consists

only of lung cancer patients. All patients of this study were outpatients and Yoshimura et al study [29] was inpatients.

In the Yellen et al study [17] the 13 item Fatigue subscale of the FACT-F demonstrated good reliability and test-retest reproducibility, suggesting an ability to be used as an independent, brief, unidimensional measure of fatigue. The same was observed in this study was that FACT-F and fatigue subscale demonstrated excellent test-retest reproducibility (0.90 for Fatigue subscale and 0.91 for Total FACT-F). Researchers and clinicians interested only in assessing fatigue as a symptom might choose to use the 13 item Fatigue subscale, whereas those interested in assessing both fatigue and quality of life would use the 40 item FACT-F [17].

Convergent validity of the Brazilian Portuguese version of the total FACT-F and Fatigue Subscale was supported by the correlation with the SF-36 (r= 0.31-0.76), and mainly vitality scale (r= 0.76).

The FACT-F has excellent known-group validity, which can accurately discriminate patients with different performance status and fatigue mean scores [17]. A lower fatigue score was associated with a reduction in activity and with increased emotional distress. Patients with high ECOG PS and patients with cancer metastasized reported lower FACT-F scores than patients with low ECOG PS and localized tumor. Post hoc comparisons (Scheffé Test) suggested that all subscales and total scores except social/family well-being were successfully discriminated between PS=0 versus 1 versus 2. This study (Table 4) and that of Yellen et al [17] and Overcash et al [30] showed that a major influencer of QOL is ECOG PS. In the Yoshimura et al [29] validation study, they

also reported significantly negative relationship between performance status and the score of the Fatigue subscale.

With regard to the limitations of this study, we had no control group to differentiate between cancer-related-fatigue and non-cancer-related fatigue. In addition, FACT was applied only in outpatients. The Brazilin sample included patients at different moments of the treatment process, presumably representing a greater variety of fatigue intensities, which could be reflected in lower average scores.

As more and more patients survive cancer, it becomes necessary to understand the multidimensional experiences of fatigue associated with the disease, treatment, and recovery process. The findings demonstrate that the FACT-F is a measure with strong psychometric properties for use in assessing fatigue and QOL in cancer patients. The FACT-F is the first instrument measuring fatigue in Brazilian cancer patients and showed excellent reliability and validity.

Conclusion

The Portuguese version of FACT-F showed high internal consistency, good test-retest reproducibility, as well as convergent validity. FACT-F successfully discriminated patients based on performance status, and clinical stage of cancer, and were positively correlated with the other measure of fatigue validated for use in Brazilian patients (SF 36 vitality scale). Therefore, the Portuguese version of FACT-F is a reliable and valid instrument to assess QOL and fatigue, representing a valid tool to screen cancer related fatigue in Brazilian

cancer patients and will allow study results to be compared across different countries.

Acknowledgements

The authors are grateful to Mr. Ben Arnold and Ms. Helen Morrow for permission to use the instrument FACT-F in this study and for having provided the questionnaire in Portuguese language. We also thank to Mrs. Sirlei Siani Morais for help in statistical review. Finally, we are grateful to all patients who participated in the study.

Authors' Disclosures of Potential Conflicts of Interest

Authors wish to disclose the absence of financial support and indicated no potential conflicts of interest.

References

1. Winningham ML, Nail LM, Burke MB, et al (1994) Fatigue and the cancer experience: the state of the knowledge. Oncol Nurs Forum 21(1): 23-36.
2. Ishikawa NM, Derchain SFM; Thuler LCS (2005) Fadiga em pacientes com câncer de mama em tratamento adjuvante. Rev Bras Cancerol 51(4): 313-318.
3. Bennett B, Goldstein D, Lloyd A, et al (2004) Fatigue and psychological distress- exploring the relationship in women treated for breast cancer. Eur J Cancer 40:1689-95.
4. Romito F, Montanaro R, Corvasce C, et al (2008) Is cancer-related fatigue more strongly correlated to haematological or to psychological factors in cancer patients? Support Care Cancer 16 (8):943-946.
5. Haghighat S, Akbari ME, Holakouei K, et al (2003) Factors predicting fatigue in breast cancer patients. Support Care Cancer 11(8):533-538.
6. Jacobsen PB, Hann DM, Azzarello LM, et al (1999) Fatigue in women receiving adjuvant chemotherapy for breast cancer: characteristics, course, and correlate. J Pain Symptom Manage 18(4):233-242.
7. Berger AM, VonEssen S, Kuhn BR, et al (2003) Adherence, sleep, and fatigue outcomes after adjuvant breast cancer chemotherapy: results of a feasibility intervention study. Oncol Nurs Forum 30(3):513-522.
8. Gurt GA. Curt GA, Breitbart W, et al (2000) Impact of cancer-related fatigue on the lives of patients: new findings from the Fatigue Coalition. Oncologist 5: 353-360.

9. Flechtner H, Bottomley A. (2003) Fatigue and Quality of Life: Lessons from the Real World. The Oncologist 8: Suppl 1, 5-9.

10. Webster K, Odom L, Peterman A, et al (1999) The Functional Assessment of Chronic Illness Therapy (FACIT) measurement system: Validation of version 4 of the core questionnaire. Quality of Life Research 8(7): 604.

11. Webster K, Cella D, Yost K. The functional assessment of chronic illness therapy measurement system: properties, applications, and interpretation. Health and Quality of Life Outcomes. 2003; 1:79.

12. Cella DF, Tulsky DS, Gray G, et al. (1993) The Functional Assessment of Cancer Therapy (FACT) scale: Development and validation of the general measure. J Clin Oncol 11(3):570-579.

13. Esper P, Mo F, Chodak G, et al (1997) Measuring Quality of life in men with prostate cancer using the Functional Assessment of Cancer Therapy-Prostate (FACT-P) instrument. Urology 50(6), 920-928.

14. Ward WL, Hahn EA, Mo F, et al (1999) Reliability and validity of the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) quality of life instrument. Qual Life Res 8(3):181-195.

15. Weitzner MA, Meyers CA, Gelke Cet al (1995) The Functional Assessment of Cancer Therapy (FACT) scale: Development of a brain subscale and revalidation of the general version (FACT-G) in patients with primary brain tumors. Cancer 75(5), 1151-161.

16. Cella DF, Bonomi AE, Lloyd SR, et al (1995) Reliability and validity of the Functional Assessment of Cancer Therapy-Lung (FACT-L) quality of life instrument. Lung Cancer 12: 199-220.

17. Yellen SB, Cella DF, Webster K, et al (1997) Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. J Pain Symptom Manage 13(2):63-74.

18. Cella D (1997) The FACT- anemia Scale. A new tool for the assessment of outcomes in cancer anemia and fatigue. Semin Hematol 34(3):13-19.

19. Eremenco SL, Cella D, Arnold BJ (2005) A Comprehensive Method for the Translation and Cross-Cultural Validation of Health Status Questionnaires. Eval Health Prof 28(2): 212-32.

20. Arnold BJ, Eremenco E, Chang CH, et al (2000) Development of a single portuguese language version of the functional assessment of cancer therapy general (FACT G) scale. Qual Life Res 9(3): 316.

21. Arnold BJ, Eremenco E, Chang CH, et al (2001) How much is “very much”? Developing a rating scale for portuguese speaking countries. Qual Life Res 10(3): 264.

22. Ware JE, Sherbourne CD. (1992) The MOS 36-item short-form health survey (SF-36) I: conceptual framework and item selection. Med Care 30(6):473-483.

23. McHorney CA, Ware JE, Raczek AE. (1993) The MOS 36-item short-form health survey (SF-36) II: psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 31(3):247-263.

24. Ciconelli RM, Ferraz MB, Santos W, et al (1999) Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida SF-36 (Brasil SF-36). Rev Bras Reumatol 39(3): 143-150.

25. Zubrod CG, Schneiderman M, Frei E III et al (1960) Appraisal of methods for the study of chemotherapy of cancer in man: comparative therapeutic trial of nitrogen mustard and thiophosphoramide. J Chronic Dis 11:7-33.

26. Cronbach LJ (1951) Coefficient alpha and the internal structure of tests. Psychometrika 16(3):297-334.

27. Nunnally JM, Bernstein IH. (1994) Psychometric theory. (3th edition). McGraw-Hill, New York.

28. Ishikawa NM, Thuler LCS, Giglio AG, et al (2008) Reproducibility of the questionnaire for assessing fatigue FACT-F in patients with cancer. Applied Cancer Research (in press).

29. Yoshimura A, Kobayashi K, Fumimoto H, et al (2004) Cross-cultural validation of the Japanese Functional Assessment of Cancer Therapy-Anemia (FACT-An). J Nippon Med Sch 71(5):314-322.

30. Overcash J, Extermann M, Parr J, et al (2001) Validity and Reliability of the FACT-G Scale for Use in the Older Person with Cancer**.** Am J Clin Oncol 24(6): 591-596.

Table 1. Demographic and Clinical Characteristics of the Validation Sample (N= 270)

Sample Characteristics	N	%
Age		
Mean ± SD (range)	50.5 ±11.8 (19-82)	
Gender		
Female	201	74.4
Male	69	25.6
Race/Ethnicity		
White	141	52.2
Black	51	18.9
Asian	2	0.7
Mulatto	76	28.2
Marital Status		
Married	146	54.1
Separated/Divorced	33	12.2
Single	56	20.7
Widowed	35	13.0
Educational Level		
= 8 year	164	60.7
9-11 years	72	26.7
> 11 years	34	12.6
Disease site		
Breast	135	50.0
Colorectal	42	15.5
Lymphoma	33	12.2
Lung	18	6.7
Sarcoma	13	4.8
Stomach	7	2.6
Testicle	5	1.9
Others *	17	6.3
Stage		
I	10	3.7
II	74	27.4
III	100	37.0
IV	86	31.9
Performance Status		
0 (fully ambulatory without physical symptoms)	85	31.5
1 (fully ambulatory with some symptoms)	148	54.8
2 (requiring <50% awake time to rest)	30	11.1
3 (requiring >50% awake time to rest)	6	2.2
4 (bedridden)	1	0.4
Treatment		
Surgery	145	53.7
Chemotherapy	270	100.0
Radiotherapy	87	32.2
Hormone therapy	11	4.1

*Others: Head and Neck (4), Myeloma (3), Ewing/PNET (2), Melanoma (3), Bladder(3), Thymoma (1), Pancreas (1).

Table 2. Internal Consistency Reliabilities and Mean of FACT-F in this Study

Subscale	(Range of Scores)	Nº of Items	Brazilian Portuguese FACT-F (N=270)	
			Mean ± SD	a
Physical	**(0-28)**	7	21.85 ± 4.86	0.78
Social/Family	**(0-28)**	7	21.12 ± 3.91	0.68
Emotional	**(0-24)**	6	19.61 ± 4.00	0.75
Functional	**(0-28)**	7	17.87 ± 5.13	0.74
Fatigue Subscale	**(0-52)**	13	39.86 ± 9.10	0.91
FACT-F	**(0-160)**	40	120.41± 20.95	0.92

FACT-F: Functional Assessment of Cancer Therapy Fatigue Scale

Table 3. Pearson Correlation between FACT-F and SF-36 Subscale Scores (Vitality Scale as an Indication of the Convergent Validity of the FACT-F) (N= 270)

	Physical FACT-F	Social FACT-F	Emotional FACT-F	Functional FACT-F	Fatigue subscale FACT-F	Total FACT-F
Physical	1.00	0.18	0.53	0.52	0.74	0.82
Social FACT-F		1.00	0.33	0.47	0.22	0.50
Emotional FACT-F			1.00	0.51	0.49	0.71
Functional FACT-F				1.00	0.58	0.80
Fatigue subscale FACT-F					1.00	0.88
SF- 36 Physical	0.23	0.14	0.11	0.33	0.30	0.31
SF- 36 Role Physical Functional	0.48	0.091	0.32	0.44	0.56	0.54
SF- 36 Body Pain	0.57	0.21	0.32	0.43	0.45	0.53
SF- 36 General Health	0.38	0.24	0.38	0.46	0.44	0.51
SF- 36 Vitality	0.65	0.25	0.56	0.52	0.77	0.76
SF- 36 Social Functioning	0.52	0.26	0.43	0.47	0.56	0.61
SF- 36 Role Emotional	0.46	0.24	0.38	0.39	0.52	0.55
SF- 36 Mental Health	0.51	0.28	0.69	0.40	0.52	0.63

FACT-F: Functional Assessment of Cancer Therapy Fatigue Scale; SF-36 MOS Short Form Health Survey.

Table 4. FACT-F Differentiation of ECOG Performance Status and Stage of Disease

Clinical Condition	N	Physical FACT-F	Social FACT-F	Emotional FACT-F	Functional FACT-F	Fatigue subscale FACT-F	Total FACT-F
Performance Status*							
0	85	24.60±2.49	21.95±3.80	20.92±2.80	20.46±4.40	45.65±4.61	133.57±12.15
1	148	21.68±4.24	20.95±3.81	19.79±3.58	17.56±4.74	39.28±8.15	119.26±18.00
=2	37	16.24±6.19	19.86±4.20	15.86±5.50	13.15±4.55	29.65±10.53	94.77±22.82
P		< 0.001	0.018	< 0.001	< 0.001	< 0.001	< 0.001
Subgroup Differences†		0>1>2	0>2	0>2, 1>2	0>1>2	0>1>2	0>1>2
Stage of Disease							
I	10	23.80±3.74	22.40±2.95	21.00±2.67	20.90±3.48	47.60±4.70	135.70±11.88
II	74	22.82±4.08	21.02±4.01	20.20±2.90	18.68±3.80	40.89±7.81	123.61±16.23
III	100	22.51±4.14	21.40±3.65	20.45±3.24	18.51±5.52	41.30±7.99	124.17±18.81
IV	86	20.03±5.82	20.72±4.19	17.97±5.13	16.07±5.36	36.72±10.62	111.51±24.53
P		< 0.001	0.470	< 0.001	< 0.001	< 0.001	< 0.001
Subgroup Differences†		I, II, III > IV	-	I, II, III > IV	I, II, III > IV	I>II, III > IV	I, II, III > IV

FACT-F: Functional Assessment of Cancer Therapy Fatigue Scale. *Performance Status: 0, fully ambulatory without physical symptoms; 1, fully ambulatory with some symptoms; 2, requiring <50% awake time to rest; 3, requiring >50% awake time to rest; 4, bedridden.

†Scheffé comparisons; > symbol separates groups that report significantly higher scores from those with lower scores.

3.3. Artigo 3

FATIGUE AND HEALTH-RELATED QUALITY OF LIFE DURING 6 CYCLES OF CHEMOTHERAPY IN BREAST CANCER PATIENTS

Neli Muraki Ishikawa, Luiz Claudio Santos Thuler, Eli Yanase, Maria de Fátima Rodrigues B Ventura, Luiz Guilherme Pinheiro Branco, and Sophie Françoise Mauricette Derchain.

Neli Muraki Ishikawa
Brazilian National Cancer Institute - INCA, Physical Therapy Department. Rua do Rezende, 128. Centro - Rio de Janeiro, RJ. Brasil CEP 20231-092. e-mail: nelimuraki@gmail.com

Luiz Claudio Santos Thuler
Federal University of the State of Rio de Janeiro - UNIRIO. Rua Mariz e Barros, 775. Maracanã - Rio de Janeiro, RJ. Brasil CEP 20270-004
e-mail: lthuler@gmail.com

Eli Yanase
Brazilian National Cancer Institute - INCA - Hospital of Cancer III, Nursing Department, Rua Visconde de Santa Isabel, 831 - Vila Isabel - Rio de Janeiro – RJ. Brasil CEP 20560-120
e-mail:

Maria de Fátima Rodrigues B Ventura
Brazilian National Cancer Institute - INCA, Hospital of Cancer III, Nursing Department, Rua Visconde de Santa Isabel, 831 - Vila Isabel - Rio de Janeiro – RJ. Brasil CEP 20560-120
e-mail:

Luiz Guilherme Pinheiro Branco
Brazilian National Cancer Institute - INCA, Hospital of Cancer III, Clinical Oncology Department, Rua Visconde de Santa Isabel, 831 - Vila Isabel - Rio de Janeiro – RJ. Brasil CEP 20560-120
e-mail:

Sophie Françoise Mauricette Derchain
Address for correspondence: Campinas State University, Department of Obstetrics and Gynecology. Rua Antônio Hossri, 629 Cidade Universitária, Campinas, São Paulo, Brazil CEP13083-370
e-mail: derchain@fcm.unicamp.br

ABSTRACT

Purpose: To assess patients before the start of chemotherapy, and after cycle 3 and 6 of chemotherapy in order to identify changes in fatigue that could occur following the initiation of chemotherapy in a sample of breast cancer patients from the Brazilian National Cancer Institute; to determine the relationship between fatigue and health related-quality of life (HRQOL); to compare fatigue and HRQOL in relation a patient's physical activity and smoking history. **Materials and methods:** 188 patients with breast cancer were included in this study with the mean age being 49.0 years. Fatigue level was measured before and during adjuvant or neoadjuvant cyclophosphamide/doxorubicin/5-fluorouracil chemotherapy regimen using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) instrument, a higher score indicates a lower level of fatigue and better HRQOL. **Results:** There was a significant decrease in mean FACT-F, fatigue subscale, FACT-G, and physical well-being scores between the start of the treatment and after cycle 3. The indications then appeared to plateau at cycle 6 reflecting maintenance in fatigue symptoms and lower quality of life in breast cancer patients. The emotional well-being scores increased slightly between the start of chemotherapy and after cycle 3 and remained a plateau at cycle 6, while social/family well-being scores showed no differences before and during chemotherapy. Fatigue was related to lower health-related quality of life. Fatigue subscale score in smoking patients decreased significantly from before and after 6 cycle of chemotherapy. FACT-G score before and after chemotherapy in active/very

active patients was slightly higher compared to sedentary/insufficiently active patients (no statistical significance). Fatigue subscale score in sedentary/insufficiently active patients decreased significantly more than active/very active patients. **Conclusions:** Fatigue increased and worsened in health-related quality of life in breast cancer submitted to chemotherapy. Fatigue affects the health related-quality of life during chemotherapy.

Keywords: Fatigue; Quality of Life; Breast Cancer; Chemotherapy

INTRODUCTION

Breast cancer is a problem of public health issue, because of its incidence and mortality. The number of new cases of breast cancer expected in Brazil in 2008 is 49.400, with an estimated risk of 51 cases for each 100 thousand women, according to estimates made by the Brazilian National Cancer Institute[1].

Technological advances in early diagnosis and treatment of cancer have increased the survival chance of patients. Increasing numbers of women are being treated with chemotherapy and recent research has shown the importance of the patient's point of view on the goals of medical care. Health-related quality of life (HRQOL) has recently become an important endpoint of clinical studies[2].

Overall, the most frequently experienced side effects in women receiving chemotherapy for breast cancer are fatigue, nausea and vomiting, taste change, and difficulty sleeping [3].

Fatigue is a major cause of reduced quality of life in cancer patients[4]. Fatigue is difficult to describe and patients express it in a variety of ways, using terms such as tired, weak, exhausted, lazy, weary, worn-out, heavy, or slow. Likewise, health professionals struggle to describe fatigue, using terms such as asthenia, lassitude, malaise, prostration, exercise intolerance, lack of energy, and weakness[5].

Fatigue is one of the most common symptoms reported by women undergoing chemotherapy or radiotherapy [6, 7] for breast cancer and may persist for months and even years following treatment [8,9]. Fatigue affects about 94% of patients with breast cancer, this frequency increasing significantly during chemotherapy and radiotherapy [10].

The cancer-related fatigue experience can include affective, cognitive, behavioral, physiological, economic, and social sequelae, making its impact on health-related quality of life multidimensional [4, 11].

The fatigue is approximately 1.5 times more severe among the former chemotherapy patients than non-cancer subjects. Former chemotherapy patients reported greater interference with their ability to work and concentrate because of fatigue, as well as greater overall interference with quality of life [12].

A large number of scales have been developed attempting to measure the nature, severity, and impact of fatigue in a range of clinical populations, and Minton and Stone[13] related 14 scales to assess fatigue, the most common questionnaires were the *Functional Assessment of Cancer Therapy Fatigue (FACT-F)*, the *European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ C30) (fatigue subscale)* and the *Fatigue Questionnaire (FQ).*

The FACT-G has been used extensively in clinic-based evaluations of individual patients. Instruments like the FACT-G, relatively brief, multidimensional questionnaires, are designed primarily for group comparisons, but individual assessment using the FACT-G has been helpful to patients and clinicians attempting to estimate change over time [14]. Because fatigue has an impact on the patient's quality of life, studies on this treatment-related side effect are of relevance to cancer management [15].

Knowledge of symptom prevalence is important in clinical practice to anticipate problems and needs of patients; to plan care for patients; and to educate clinical staff to focus on particular symptoms[16]. This is the first study that assesses the fatigue in Brazilian breast cancer patients during the adjuvant and neoadjuvant

chemotherapy using FACT-F and it is important to know the fatigue symptom to establish an effective care system for patients.

The purpose of this study was (1) to assess patients before the start of chemotherapy, and after cycle 3 and 6 of chemotherapy in order to identify changes in fatigue and quality of life that could occur following the initiation of chemotherapy in a sample of breast cancer patients from the Brazilian National Cancer Institute; (2) to determine the relationship between fatigue and HRQOL; and (3) to compare fatigue and HRQOL in relation a patient's physical activity and smoking history.

PATIENTS AND METHODS

This study was prospective and longitudinal in design. Breast cancer patients in the Clinical Oncology Department of the Brazilian National Cancer Institute with stage II or III referred to receive a minimum of six cycles of adjuvant or neoadjuvant chemotherapy with cyclophosphamide/doxorubicin/5-fluorouracil (CAF) regimen were invited to participate. Neoadjuvant patients received CAF chemotherapy after a biopsy to confirm invasive disease and after clinical staging. Adjuvant patients received CAF chemotherapy after clinical staging and definitive surgical treatment with either lumpectomy or mastectomy. Consecutive sampling was used to accrue the sample. Data was collected between January 2006 and March 2007.The inclusion criteria were to be 30-70 years old and to have a *performance status* rating of 0-2. Exclusion criteria included: pregnancy; subjects with more than one diagnosis of cancer; history of treatment with radiotherapy; and patients with a psychiatric diagnosis and have chronic pulmonary disease and severe cardiac disorders. Data collection occurred prospectively over 3 points in time, FACT-F questionnaires

were completed before starting cycle 1 of chemotherapy and after cycle 3 and 6 of chemotherapy. 188 participants were included in this study, of whom 11 (5.9%) had progression of the disease and had changed their treatment plans, and 20 (10.6%) didn't complete 6 cycles of chemotherapy (discontinued participation in the study prior to completing all assessments). The final sample for analysis consisted of 157 patients.

This study was approved by the Research Ethics Committee of the Brazilian National Cancer Institute; participation was voluntary and a written informed consent was obtained during an outpatient Clinic Oncology visit prior to the start of chemotherapy and before completion of the instrument. Eligible breast cancer patients were asked to participate in a brief interview designed to elicit a variety of information using a structured interview format pertinent to sociodemographic information. The disease and treatment information was also collected from the patient's medical file.

Measures

The questionnaire administered to all participants included the FACT-F [17, 18], and Eastern Cooperative Oncology Group (ECOG) Performance Status Rating [19].

Functional Assessment of Cancer Therapy-Fatigue (FACT-F) [17,18], version 4 consists of a 40 item self-report instrument that includes 40 likert-type items in 4 scale that assesses a quality of life across the domains of physical well-being (seven items), which is the patient's actual physical experience of a disease and/or treatment, including disease symptoms and treatment side effects; social/family well-being (seven items), which encompasses activities with and support from

family and friends; emotional well-being (six items), which refers not only to emotional distress, but also to positive well-being or life happiness; and functional well-being (seven items), which refers to a person's ability to engage in the usual basic activities of daily living**;** and one scale with 13 item fatigue that assesses fatigue with scores ranging from 0 to 52. Subjects were asked to respond to each item with a score from 0 to 4, where 0=not all, 1=a little bit, 2=somewhat, 3=quite a bit, and 4=very much. The possible range of scores is from 0 to 160. A higher score indicates a lower level of fatigue and better HRQOL. FACT-F was validated to the Portuguese in Brazilian cancer patients[21] and showed high internal consistency (Cronbach a coefficient was 0.78 for physical well-being, 0.68 for social/family well-being, 0.75 for emotional well-being, 0.74 for functional well-being, 0.91 for fatigue subscale, and 0.92 for total FACT-F and good test-retest reproducibility (intraclass correlation 0.72 - 0.91).

The *Eastern Cooperative Oncology Group (ECOG) Performance Status (PS)*[19] is a five-point scale ranging scores from 0 (fully ambulatory without physical symptoms), 1 (fully ambulatory with some symptoms), 2 (requiring <50% awake time to rest), 3 (requiring >50% awake time to rest), to 4 (bedridden). It is widely used in cancer patient trials to assess functional capability of patients as they undergo treatment. It is used as an independent prognostic predictor in patients with cancer. The ECOG PS item was included because it is a familiar, somewhat global index.

The *Demographic and Disease Information* is a demographic information sheet that covers basic patient information such as age, race/ethnicity, educational level, marital status, levels of physical activity, and smoking history.

Levels of physical activity was classified[20] in: Very Active: = 30 minutes/session of vigorous activity = 5 days/week; and/or = 20 minutes/session of vigorous activity = 3 days/week added up to = 30 minutes/session of moderate activities or walking = 5 days/week; Active: = 20 minutes session of vigorous activity = 3 days/week, and/or activities of moderate activities or walking = 5 days/week or = 150 minutes per week of any activities; Insufficiently; Active**:** < 150 minutes/week and > 10 minutes/week of any activities; and Sedentary**:** = 10 minutes per week of any activities.

Smoking history was classified in: non-smoker, former smoker and current smoker. A disease sheet covers the stage of disease, treatment status and body mass index.

Statistical Methods/Analysis

Statistical Package for the Social Sciences (SPSS) version 13.0 was used for all statistical analyses. The Wilcoxon signed ranks test was performed to evaluate differences between before starting cycle 1 of chemotherapy and after cycle 3, and after cycle 3 and 6 of chemotherapy; to compare groups of patients between neoadjuvant versus adjuvant chemotherapy, with decreased, unchanged, and increased fatigue and health-related quality of life at a given measurement; and to compare fatigue and HRQOL in relation a patient's physical activity and smoking history.

Pearson's correlation coefficients were used to examine the relationship between fatigue subscale scores and FACT-G scores (total and in the different domains) to time before chemotherapy, after cycle 3, and after cycle 6. Pearson

correlation coefficient was classified in the following way: 0-0.25 - not correlated; 0.25-0.50 - weak correlation; 0.50-0.75 - moderated to good correlation; >0.75 very good to excellent correlation [22].

For all tests, a significance level of 0.05 was chosen, and all p were two-tailed.

RESULTS

One hundred seven patients completed 6 cycles of cyclophosphamide /doxorubicin/5-fluorouracil (CAF) chemotherapy in current study, 84 (53.5%) were white and 79 (50.3%) were married. The mean age of the patients was 49.0 years, with a range of 30-69 years; 90 (57.3%) had attended = 8 year of educational level; 76 had stage IIIB (48.4%); 108 had performance status 1 (68.8%). All patients received CAF regimens of chemotherapy, 99 (62.4%) were in neoadjuvant chemotherapy regimen; 38 (24.2%) had mastectomy; 104 (66.2%) were non-smoker; 131 (83.4%) were sedentary, and the mean body mass index was 28.1 with a range of 16.6 - 41.2 Kg/m^2. No patient received concurrent chemoradiotherapy. Demographic and clinical information is available in Table 1.

The mode of administration of the FACT-F (self-administration vs. read in interview) was registered in 157 cases, although the FACT-F was designed for self-administration, 79 patients (50.3%) in our sample were interviewed due to low educational level.

As shown in Table 2, there was a significant decrease in mean FACT-F, fatigue subscale, FACT-G, and physical well-being scores between the start of the treatment and after cycle 3 and then appeared to plateau at cycle 6 reflecting maintenance in fatigue symptoms and lower quality of life in breast cancer

patients. The emotional well-being scores increased a little between the start of chemotherapy and after cycle 3 and remained a plateau at cycle 6, while social/family well-being and functional well-being scores showed no differences before and during chemotherapy.

Pearson correlation of scores was obtained between fatigue subscale and FACT-G (total and in the different domains) to time before chemotherapy, after cycle 3, and after cycle 6. Values found for Pearson correlation between fatigue subscale and FACT-G were r=0.58 before chemotherapy, r=0.75 after cycle 3, and r=0.75 after cycle 6; fatigue subscales between physical well-being was r=0.57 before chemotherapy, r=0.81 after cycle 3, and r=0.87 after cycle 6; fatigue subscales between social/family well-being were r=0.32 before chemotherapy, r=0.21 after cycle 3, and r=0.29 after cycle 6; fatigue subscales between emotional well-being were r=0.28 to before chemotherapy, r=0.54 after cycle 3, and r=0.45 after cycle 6; and fatigue subscales between functional well-being were r=0.51 before chemotherapy, r=0.66 after cycle 3, and r=0.69 after cycle 6.

Figure 1 shows the differences in fatigue subscale and FACT-G scores between physical activity with sedentary/insufficiently active (n=141), and active/very active patients (n=16); before cycle1 and after cycles 3 and 6. FACT-G scores in sedentary/insufficiently active patients decreased from 80.2±11.1 to 78.5±12.9 (p value=0.13) after cycle 3 and to 78.3±14.7 (p value=0.305) after cycle 6, while for active/very active patients from 89.0±11.1 to 80.47±21.9 (p value=0.01) after cycle 3 and to 84.6±15.8 (p value=0.09) after cycle 6. This fall showed no statistical significance. In contrast, Fatigue subscale score in sedentary/insufficiently active patients decreased from 45.7±4.6 to 39.7 ±9.3 (p value<0.001) after cycle 3 and

to 39.3±10.9 (p value<0.001) after cycle 6, while for active/very active patients score from 46.6 ±7.1 to 39.3±14.4 (p value=0.01) after cycle 3 and to 42.0±9.6 (p value=0.07) after cycle 6.

We compared fatigue subscale and FACT-G scores before and after cycle 6 of chemotherapy, for patients with smoking history (non-smoker n=138; smoker n=19). FACT-G scores for non-smoker decreased from 80.8±11.9 before chemotherapy to 78.6±15.3 (p=0.145) after cycle 6, while for smoker patients the score decreased from 83.4±7.2 to 81.2±11.8 (p=0.904) after cycle 6 chemotherapy. In contrast, fatigue subscale in non-smoker patients decreased significantly from 45.7±5.1 to 39.8±10.4 (p value<0.001), while for smoker patients the score decreased from 46.5 ±3.1 to 37.8±14.0 (p value=0.035).

Our sample was 157 patients with 99 patients submitted to neoadjuvant chemotherapy and 58 to adjuvant chemotherapy. Values found for FACT-G scores in neoadjuvant patients before chemotherapy were 82.1±11.4, 79.9±14.1 after cycle 3 and 78.5±14.7 after cycle 6. In adjuvant patients FACT-G scores were 79.4±11.5, 76.5±13.7 after cycle 3, and 79.7±15.3 after cycle 6. Values found for fatigue subscale scores in neoadjuvant patients before chemotherapy were 46.4±5.1, 40.4±9.7 after cycle 3, and 39.2±11.0 after cycle 6. In adjuvant patients fatigue subscale scores were 44.6±4.4, 38.6±10.0 after cycle 3, and 40.1±10.7 after cycle 6. Figure 2 presents the differences in fatigue subscale and FACT-G scores between neoadjuvant and adjuvant chemotherapy patients.

According to Body Mass Index (BMI), patients with BMI<25 (n=42), BMI 25-29.9 (n=61) and BMI = 30 (n=54) were compared to fatigue subscale and FACT-G

and there were no significant differences in scores before chemotherapy, and after cycle 3 and cycle 6.

DISCUSSION

Fatigue is one of the most common symptoms reported by women undergoing chemotherapy. This study assessed patients before the start of chemotherapy, and after cycles 3 and 6 of chemotherapy in order to identify changes in fatigue that could occur following the initiation of chemotherapy in a sample of breast cancer patients from the Brazilian National Cancer Institute. In this study FACT-F, FACT-G, fatigue subscale, and physical well-being mean scores of breast cancer patients after cycle 3 of chemotherapy were significantly lower compared to the start of chemotherapy. No significant difference was found in fatigue and health quality of life between cycle 3 and cycle 6 of chemotherapy.

The common perception among patients and nurses that fatigue increase over time while patients receive chemotherapy treatments was not supported by Berger's study [23]. De Jong et al[24] found in a literature review that fatigue in patients with breast cancer receiving adjuvant chemotherapy was high and fluctuating rates of fatigue during and after adjuvant chemotherapy and the intensity of fatigue seems to be stable throughout the treatment cycles. The explanation is that patients become accustomed to fatigue[24]. Some studies have shown similar observation, and were evaluated in patients submitted to four cycles of chemotherapy regimens. Berger [23] showed in 72 women receiving chemotherapy after surgery in stage I-II breast cancer, fatigue levels 48 hours after each of the first 3 chemotherapy cycles were not significantly different over time. Jacobsen et al [25] also reported similar results in stage

I-III breast cancer patients; the prevalence and severity of fatigue significantly increased after the start of chemotherapy and remained elevated during the following three cycles. Donovan et al [26] assessed fatigue in 134 women at the start of their first, third, and final cycles of chemotherapy. Fatigue severity increased significantly from the start of chemotherapy to the middle of chemotherapy but did not change significantly from the middle of chemotherapy to the end of chemotherapy. Byar et al [27] analyzed 25 women, with stage I-II breast cancer before and after receiving doxorubicin-based chemotherapy, fatigue levels were moderately intense during treatments and did not rise with subsequent treatments. Payne et al [28] assessed fatigue in four measurement points (during cycles 1 and 4 on days 1–3 and at the two-week nadir points). The mean changes in fatigue scores did not differ significantly between cycles 1 and 4. Interestingly, no progressive increase in fatigue score was found over the course of the four cycles of chemotherapy.

However, Berger and Higginbotham [29] studied in a pilot study with 14 breast cancer patients, with stage I or II, during and after doxorubicin and cyclophosphamide chemotherapy, patients experienced the highest levels of fatigue and symptom distress during the first four days after treatment 3 of chemotherapy. Kumar et al [30] studied 198 consecutive breast cancer patients receiving adjuvant chemotherapy, who were monitored from start to end of chemotherapy. Ninety four percent (94%) of all patients reported increased frequency of fatigue at end of treatment, compared to 42% at start of treatment as measured by the Fatigue Symptom Scale. Liu et al [31] showed in 63 women with stage I–IIIA breast cancer in four cycles of adjuvant or neoadjuvant anthracycline-based chemotherapy that fatigue significantly increased from baseline to cycle 1. Fatigue of cycle 4 was significantly

higher than during baseline and significantly higher than cycle 1. Data was collected before and during weeks 1, 2, and 3 of cycle 1 and cycle 4.

Our study evaluated fatigue in breast cancer patients that submitted 6 cycles of chemotherapy, and few studies evaluated a fatigue in patients with more than four cycle of chemotherapy. De Jong et al [32] reported fatigue in a sample of 157 patients with breast cancer, they were interviewed at the first, third and fifth cycle of adjuvant chemotherapy. Patients were treated with doxorubicin-containing schedule, or cyclophosphamide, methotrexate and 5-fluorouracil (CMF). After the start of chemotherapy, a direct increase in fatigue was seen in the doxorubicin group, whereas the increase in the CMF group does not show until after the fifth cycle of chemotherapy. The fatigue experienced at the first and the last measurements do not differ significantly. In another study of De Jong et al [33] course of mental fatigue and motivation varied, but seemed to be stable during the treatment of chemotherapy. In Zachariae et al [34] study fatigue was measured before 1st cycle of chemotherapy, at 4, 6, and last cycle. The women reported significant increases in fatigue during treatment with increased fatigue found after all subsequent cycles compared to cycle 1.

To determine if there are differences in neoadjuvant versus adjuvant chemotherapy in the sample, we found that FACT-G scores in neoadjuvant patients were slightly higher than in adjuvant patients, and the same was with fatigue subscale score (not significant). FACT-G scores in neoadjuvant group significantly decreased after cycle 6. In adjuvant patients FACT-G scores decreased after cycle 3 and returned to the same value compared with before chemotherapy. Fatigue score in neoadjuvant and adjuvant patients decreased significantly

compared with before chemotherapy. Reason for the increased fatigue in patients before the start of chemotherapy was the physical and psychological stress associated with those having recently undergone breast cancer surgery [25].

In this study, our sample received only cyclophosphamide, doxorubicin, and fluorouracil (CAF) chemotherapy regimens. The differences in chemotherapy regimens on the course of fatigue are unclear. Berger and Walker[35] found that chemotherapy protocols which contain intravenous doxorubicin were directly associated with higher fatigue at the first chemotherapy treatment. De Jong et al [32] reported that the course of fatigue during and after chemotherapy treatment was significantly different for the CMF group, compared with the doxorubicin group. Jacobsen et al [25] concluded that fatigue was not influenced by the chemotherapy regimens (doxorubicin, doxorubicin and cyclophosphamide (AC), CAF, or doxorubicin, cyclophosphamide, and methotrexate). And a similar result was found in Liu et al study [31] that reported no significant differences with different chemotherapy with AC; CAF; AC plus docetaxel; AC plus paclitaxel; with cyclophosphamide, epirubicin, and fluorouracil (CEF) regimens in any of the analyses. Fatigue scores were significantly higher in women on 28-day chemotherapy cycles (CAF, CMF) than in women on 21-day cycles at the midpoints of the first and third treatments, but not at the second midpoint [23].

In the present study, Fatigue subscale showed a moderate Pearson's correlation coefficient with FACT-G after cycle 3 and cycle 6 ($r= 0.75$, $p< 0.001$). Pearson's correlations coefficient with fatigue subscale and physical well-being subscale was excellent after cycle 3 ($r=0.81$, $p< 0.001$) and $r=0.87$ ($p< 0.001$) after cycle 6. This high relation with fatigue and the physical well-being during

chemotherapy showed that as low was the physical condition, worst is the fatigue, increasing the correlation after cycles 3 and 6 of chemotherapy. A moderated to good correlation (r=0.50-0.75) showed for fatigue subscale and functional well-being to time before chemotherapy and an increase at cycle 3 and 6 of chemotherapy indicated that fatigue interferes in daily activities during chemotherapy.

Findings were also consistent with literature that reported that women's higher fatigue is related to lower HRQOL[15, 36, 37, 27]. Fatigue was correlated with greater symptom distress [29] emotional domain and mental domain[27], poorer physical [27, 29, 36] , social health status [29], health [38] and functioning subscale [32, 35, 36, 38]. This included difficulty to start and finish tasks, to be too tired to act, needing help with activity, and frustration [36]. Compared to women with no history of cancer, women receiving chemotherapy reported that fatigue interfered to a greater extent with their general activity, ability to bathe and dress, normal work activity, ability to concentrate, relations with others, enjoyment of life, and mood[25].

The association between fatigue and impaired physical functioning can be explained in a number of ways. Patients who feel exhausted probably reduce their physical activity in order to minimize their discomfort. Indeed, reduced activity is one of the ways in which individuals gauge the severity of their fatigue[39].

This study showed a weak correlation (r=0.25-0.50) for fatigue subscale and emotional well-being to time before chemotherapy an increase at cycles 3 and 6 of chemotherapy indicated that fatigue was related with emotional symptoms during chemotherapy. There were no significant changes in correlation between fatigue and social/family well being during chemotherapy. Social and emotional well-being are very important to quality of life, they are not as likely to change as

quickly or dramatically over time or in response to physical health interventions such as pharmaceutical treatments in clinical trials[14].

Although many cancer studies have examined fatigue during and after chemotherapy, only a small number evaluated the association between smoking and fatigue [40, 41]. The results of the current study also showed that fatigue subscale score in smoking patients decreased significantly from before and after 6 cycle of chemotherapy.

In this study the FACT-G score before and after chemotherapy in active/very active patients was slightly higher compared to sedentary/insufficiently active patients (no statistical significance). In contrast fatigue subscale score in sedentary/insufficiently active patients decreased significantly more than in active/very active patients. Researchers have found that women who report less physical activity during or after treatment report greater levels of fatigue [23, 29]. Reduced activity may itself contribute to the development of fatigue via the mechanism of deconditioning [42].

Fatigue intensity should be monitored closely by health professionals, and patients need to know that fatigue can compromise their quality of life. Efforts should be aimed at the development and evaluation of interventions to reduce or minimize the impact of chemotherapy on fatigue, other symptoms, and QOL. Likewise, there is growing evidence that interventions designed to increase activity levels have had beneficial effects on fatigue in cancer patients [43]. In terms of interventions, physical therapists can teach patients management strategies such as how to schedule treatments, plan realistically for periods of rests, and seek support from family when needed [44] . The reason why only some patients develop significant

fatigue is not known. Physical exercise programs have been shown to be effective in reducing the cancer-related fatigue [45, 46, 47].

Strength of the current study is its longitudinal design, repeated assessments during the course of chemotherapy, and breast cancer patients received only one chemotherapy regimens (CAF) for 6 cycles. However, we assessed fatigue three times, and data was collected in different days, before chemotherapy, between 3 and 4 cycles, and after cycle 6. This assessment schedule may have obscured more meaningful day-to-day fluctuations in fatigue.

CONCLUSION

There was a significant decrease in mean FACT-F, fatigue subscale, FACT-G, physical well-being scores between the start of the treatment and after cycle 3 and then appeared a plateau at cycle 6 reflecting maintenance in fatigue symptoms and lower quality of life in breast cancer patients during 6 cycles of CAF chemotherapy in our Institute. Fatigue was related to lower HRQOL. Fatigue subscale score in smoking patients decreased significantly comparing before and after cycle 6 of chemotherapy. FACT-G score before and after chemotherapy in active/very active patients was higher compared to sedentary/insufficiently active patients (no statistical significance). In contrast fatigue subscale score in sedentary/insufficiently active patients decreased significantly more than active/very active patients.

The study results provide directions for assessment and monitoring fatigue in breast cancer patients undergoing chemotherapy.

ACKNOWLEDGEMENTS

The authors are grateful to Mr. Ben Arnold and Ms. Helen Morrow for permission to use the instrument FACT-F in this study and for having provided the questionnaire in Portuguese language. Finally, we are grateful to all patients who participated in the study.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Authors wish to disclose the absence of financial support and off-label or investigational use of drugs or devices for this study. The authors indicated no potential conflicts of interest.

REFERENCES

1. Instituto Nacional de Câncer (INCA). Estimativas 2008: Incidência de Câncer no Brasil. Rio de Janeiro: INCA, 2007.
2. Kuroi K, Shimozuma K, Ohsumi S, et al. Current Status of Health Outcome Assessment of Medical Treatment in Breast Cancer. Breast Cancer. 2007, 14 (1): 74-80.
3. Williams SA, Schreier AM. The Effect of Education in Managing Side Effects in Women Receiving Chemotherapy for Treatment of Breast Cancer. Oncol Nurs Forum. 2004, 31(1): E16–E23. Digital Object Identifier: 10.1188/04. ONF. E16-E23.
4. Curt GA, Breitbart W, Cella D, et al. Impact of cancer-related fatigue on the lives of patients: new findings from the fatigue coalition. Oncologist. 2000, 5: 353–360.

5. National Cancer Institute (NCI) [homepage on the Internet]. United States: National Institutes of Health Fatigue (PDQ®): Overview. Available from: http://www.cancer.gov/cancertopics/pdq/supportivecare/fatigue/HealthProfessional/page2, Accessed 09/09/2008.
6. Wratten C, Kilmurray J, Nash S, et al. Fatigue during breast radiotherapy and its relationship to biological factors. Int J Radiat Oncol Biol Phys. 2004, 59(1):160-7.
7. Fürst CJ, Ahsberg E. Dimensions of fatigue during radiotherapy. An application of the Multidimensional Fatigue Inventory. Support Care Cancer. 2001, Jul; 9(5): 355-60.
8. Bower JE, Ganz PA, Desmond KA, et al. Fatigue in breast cancer survivors: occurrence, correlates, and impact on quality of life. Clin Oncol. 2000, 18(4):743-53.
9. Kim SH, Son BH, Hwang SY, et al. Fatigue and depression in disease-free breast cancer survivors: prevalence, correlates, and association with quality of life. J Pain Symptom Manage. 2008, 35(6):644-55.
10. Ishikawa NM, Derchain SFM; Thuler LCS. Fadiga em pacientes com câncer de mama em tratamento adjuvante. Rev Bras Cancerol. 2005, 51(4):313-318.
11. Portenoy RK, Itri LM. Cancer-related fatigue: guidelines for evaluation and management. Oncologist. 1999, 4(1):1-10.
12. Broeckel JA, Jacobsen PB, Horton J, et al. Characteristics and correlates of fatigue after adjuvant chemotherapy for breast cancer. J Clin Oncol. 1998, 16(5):1689-96.
13. Minton O, Stone P. A systematic review of the scales used for the measurement of cancer-related fatigue (CRF). Ann Oncol. Access published August 4, 2008, doi:10.1093/annonc/mdn537.

14. Webster K, Cella D, K Yost. The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: properties, applications, and interpretation. Health Qual Life Outcomes. 2003, 1:79.
15. Visser MR, Smets EM. Fatigue, depression and quality of life in cancer patients: how are they related? Support Care Cancer. 1998, 6(2):101-8.
16. Higginson IJ, Addington-Hall JM. The epidemiology of death and symptoms. In: Doyle D, Hanks G, Cherny N, Calman K, eds. Oxford textbook of palliative medicine, 3rd ed. Oxford: Oxford University Press, 2003: 14-24.
17. Yellen SB, Cella DF, Webster K, et al. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. J Pain Symptom Manage. 1997, 13(2):63-74.
18. Cella D. The FACT- anemia Scale. A new tool for the assessment of outcomes in cancer anemia and fatigue. Semin Hematol. 1997, 34(3):13-19.
19. Zubrod CG, Schneiderman M, Frei E, et al. Appraisal of methods for the study of chemotherapy of cancer in man: comparative therapeutic trial of nitrogen mustard and thiophosphoramide. J Chronic Dis. 1960, 11:7-33.
20. Craig CL, Marshall AL, Sjöström M, et al. International Physical Activity Questionnaire: 12-Countr reliability and validity. Med Sci Sports Exerc. 2003, 35:1381-95.
21. Ishikawa NM, Thuler LCS, Giglio AG, et al. Validation of the Portuguese Version of Functional Assessment of Cancer Therapy-Fatigue (FACT-F) in Brazilian Cancer Patients. Support Care Cancer. 2008 (in press).
22. Colton T. 1974 Statistics in Medicine (p 211) Boston: Little, Brown and Company.

23. Berger AM. Patterns of fatigue and activity and rest during adjuvant breast cancer chemotherapy. Oncol Nurs Forum. 1998, 25(1):51-62.

24. De Jong N, Courtens AM, Abu-Saad HH, et al. Fatigue in patients with breast cancer receiving adjuvant chemotherapy: a review of the literature. Cancer Nurs. 2002, 25(4):283-97.

25. Jacobsen PB, Hann DM, Azzarello LM, et al. Fatigue in women receiving adjuvant chemotherapy for breast cancer: characteristic, course, and correlates. J Pain Symptom Manage. 1999, 18:233–242.

26. Donovan KA, Jacobsen PB, Andrykowski MA, et al. Course of Fatigue in Women Receiving Chemotherapy and/or Radiotherapy for Early Stage Breast Cancer. J Pain Symptom Manage. 2004, 28 (4): 373-380.

27. Byar KL, Berger AM, Bakken SL, et al. Impact of Adjuvant Breast Cancer Chemotherapy on Fatigue, Other Symptoms, and Quality of Life. Oncol Nurs Forum. 2006, 33(1):E18-E26.

28. Payne JK, Piper BF, Rabinowitz I, et al. Biomarkers, Fatigue, Sleep, and Depressive Symptoms in Women with Breast Cancer: A Pilot Study. Oncol Nurs Forum. 2006, 33(4): 775-783.

29. Berger AM, Higginbotham P. Correlates of fatigue during and following adjuvant breast cancer chemotherapy: a pilot study. Oncol Nurs Forum. 2000, 27(9):1443-8.

30. Kumar N, Allen KA, Riccardi D, et al. Fatigue, weight gain, lethargy and amenorrhea in breast cancer patients on chemotherapy: is subclinical hypothyroidism the culprit? Breast Cancer Res Treat. 2004, 83: 149–159.

31. Liu L, Marler MR, Parker BA, et al. The relationship between fatigue and light exposure during Chemotherapy. Support Care Cancer. 2005, 13(12): 1010–1017.
32. De-Jong N, Candel MJJM, Schouten HC et al. Prevalence and course of fatigue in breast cancer patients receiving adjuvant chemotherapy. Ann Oncol. 2004, 15: 896–905.
33. De Jong N, Candel MJJM, Schouten HC, et al. Course of mental fatigue and motivation in breast cancer patients receiving adjuvant chemotherapy. Ann Oncol. 2005, 16: 372–382.
34. Zachariae R, Paulsen K, Mehlsen M, et al. Pretreatment distress and posttreatment nausea, vomiting, and fatigue were assessed at the 1st, 4th, 6th and last cycles of chemotherapy. Psychother Psychosom. 2007, 76:376–384.
35. Berger A, Walker SN. An explanatory model of fatigue in women receiving adjuvant breast cancer chemotherapy. Nurs Res. 2001, 50: 43–54.
36. Tchen N, Juffs HG, Downie FP, et al. Cognitive Function, Fatigue, and Menopausal Symptoms in Women Receiving Adjuvant Chemotherapy for Breast Cancer. J Clin Oncol. 2003, 21:4175-4183.
37. Mills PJ, Parker B, Dimsdale JE. The relationship between fatigue and quality of life and inflammation during anthracycline-based chemotherapy in breast cancer. Biol Psychol. 2005, 69: 85-96.
38. Gupta D, Lis CG, Grutsch JF. The Relationship between Cancer-Related Fatigue and Patient Satisfaction with Quality of Life in Cancer. J Pain Symptom Manage. 2007, 34 (1):40-47.

39. Stone P, Richards M, A'Hern R, et al. Fatigue in Patients with Cancers of the Breast or Prostate Undergoing Radical Radiotherapy. J Pain Symptom Manage. 2001, 22(6):1007-1015.
40. Ng AK, Li S, Recklitis C, et al. A comparison between long-term survivors of Hodgkin's disease and their siblings on fatigue level and factors predicting for increased fatigue. Ann Oncol. 2005, 16(12):1949-55.
41. Prieto JM, Blanch J, Atala J, et al. Clinical factors associated with fatigue in haematologic cancer patients receiving stem-cell transplantation. Eur J Câncer. 2006, 42:1749 –55.
42. Winningham ML, Nail LM, Burke MB, et al. Fatigue and the cancer experience: the state of the knowledge. Oncol Nurs Forum. 1994, 21:23–36.
43. Irwin ML, Ainsworth BE. Physical Activity Interventions Following Cancer Diagnosis: Methodologic Challenges to Delivery and Assessment. *Cancer Investigation.* 2004, 22(1): 30-50.
44. Hoskins CN. Breast cancer treatment-related patterns in side effects, psychological distress, and perceived health status. Oncol Nurs Forum. 1997, 24(9):1575-83.
45. Heim ME, Malsburg MLE, Niklas A. Randomized Controlled Trial of a Structured Training Program in Breast Cancer Patients with Tumor-Related Chronic Fatigue. Onkologie. 2007, 30:429–34.
46. Pinto BM, Frierson GM, Rabin C, et al. Home-Based Physical Activity Intervention for Breast Cancer Patients. J Clin Oncol. 2005, *23*:3577–87.
47. Watson T, Mock V. Exercise as an intervention for cancer-related fatigue. *Phys Ther*. 2004, 84: 736 –743.

Table 1. Demographic and Clinical Characteristics of Study Sample (n= 157)

Sample Characteristics	N	%
Age		
Mean ± SD (range)	49.0 ±8.6 (30-69)	
Race/Ethnicity		
White	84	53.5
Black	28	17.8
Mulatto	45	28.7
Marital Status		
Married	79	50.3
Separated/Divorced	25	15.9
Single	39	24.8
Widowed	14	8.9
Educational Level		
= 8 Year	90	57.3
9-11 Years	50	31.8
> 11 Years	17	10.8
Stage of Disease at Diagnosis		
IIA	16	10.2
IIB	35	22.3
IIIA	30	19.1
IIIB	76	48.4
Performance Status		
0 (fully ambulatory without physical symptoms)	47	29.9
1 (fully ambulatory with some symptoms)	108	68.8
2 (requiring <50% awake time to rest)	2	1.3
Treatment		
Surgery		
Mastectomy	38	24.2
Lumpectomy	20	12.7
No Surgery	99	63.1
Chemotherapy		
Adjuvant	58	37.6
Neoadjuvant	99	62.4
Smoking History (tobacco habits)		
Non-Smoker	104	66.2
Former Smoker	34	21.7
Current Smoker	19	12.1
Levels of Physical Activity		
Sedentary	131	83.4
Insufficiently Active	10	6.4
Active	9	5.7
Very Active	7	4.5
Body Mass Index (Kg/m^2)		
Mean ± SD (range)	28.1 ±5.0 (16.6-41.2)	

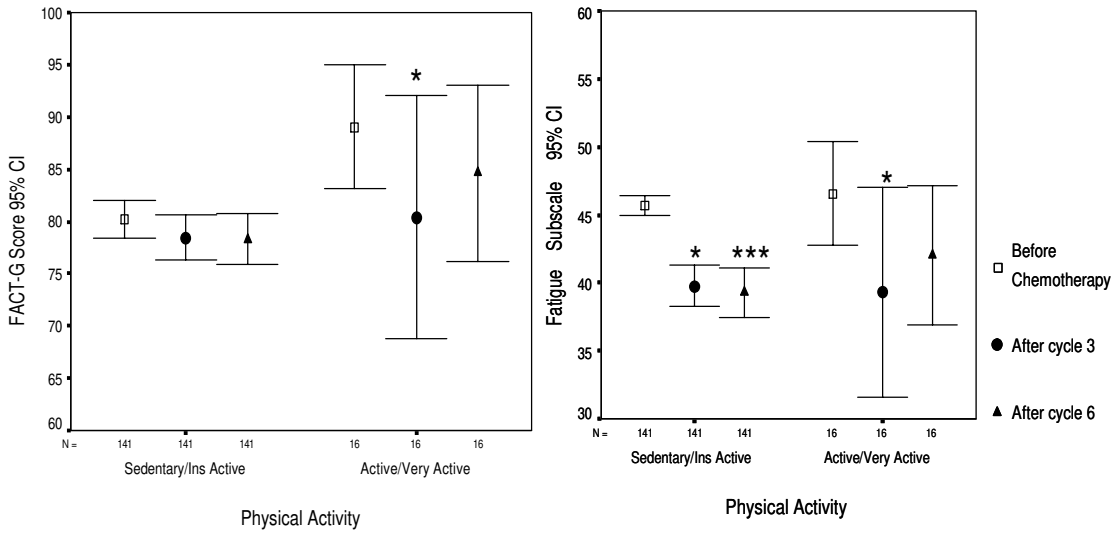
Table 2. FACT-F and Subscales Scores Before Chemotherapy, and After Cycle 3 and 6 (N=157)

	Before Chemo (A)		After Cycle 3 (B)		p Value (AXB)	After Cycle 6 (C)		p Value** (BXC)	p Value*** (AXC)
	Mean (SD)	Range	Mean (SD)	Range		Mean (SD)	Range		
FACT-F (0-160)	126.8 (14.8)	81-159	118.3 (22.4)	19-156	**<0.001[a]**	118.5 (24.1)	38-154	0.849	**<0.001[a]**
Fatigue subscale (0-52)	45.8 (4.9)	21-52	39.7 (9.8)	1-52	**<0.001[a]**	39.6 (10.8)	4-52	0.586	**<0.001[a]**
FACT-G (0-108)	81.1 (11.4)	53-107	78.6 (14.0)	18-104	**0.029[a]**	78.9 (14.9)	25-102	0,698	0.151
Physical well being (0-28)	24.3 (3.3)	12-28	20.4 (5.7)	0-28	**<0.001[a]**	21.3 (5.6)	3-28	0.108	**<0.001[a]**
Social/family well being (0-28)	20.8 (4.1)	6-28	20.9 (4.2)	6-28	0.839	20.4 (4.3)	5-28	0.055	0.194
Emotional well being (0-24)	17.8 (4.2)	4-24	19.7 (3.5)	6-24	**<0.001[a]**	19.7 (3.7)	4-24	0.802	**<0.001[a]**
Functional well being (0-28)	18.1 (4.5)	6-28	17.7 (4.7)	2-28	0.116	17.6 (4.9)	3-28	0.999	0.260

Abbreviations: FACT-F= Functional Assessment of Cancer Therapy-Fatigue; FACT-G= Functional Assessment of Cancer Therapy-General; SD= Standard Deviation.

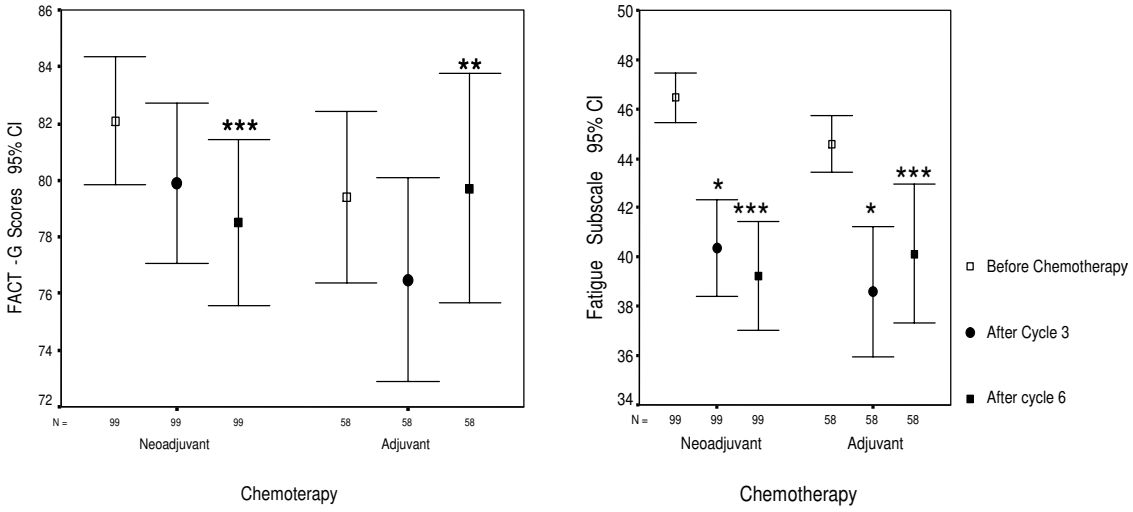
Note: higher scores represent better function. Test statistics= Wilcoxon Signed Ranks Test, *before versus after cycle 3, ** after cycle 3 versus after 6, *** before versus after cycle 6. [a]=statistically significant results are bold.

Figure 1. Fatigue Subscale and FACT-G Before Chemotherapy and After Cycle 3 and Cycle 6, for Physical Activity



Abbreviations: FACT-G = Functional Assessment of Cancer Therapy-General. Test statistics= Wilcoxon Signed Ranks Test. Statistically significant= *before versus after cycle 3, ** after cycle 3 versus after 6, *** before versus after cycle 6.

Figure 2. Fatigue Subscale and FACT-G Before Neoadjuvant/Adjuvant Chemotherapy, and After Cycle 3 and Cycle 6



Abbreviations: FACT-G = Functional Assessment of Cancer Therapy-General. Test statistics= Wilcoxon Signed Ranks Test. Statistically significant= *before versus after cycle 3, ** after cycle 3 versus after 6, *** before versus after cycle 6.

4. Discussão

A disponibilidade do FACT-F validado em língua portuguesa é relevante quanto aos aspectos científicos na área de pesquisa, uma vez que possibilita avaliar a fadiga e qualidade de vida em pacientes com câncer em relação à prevalência, incidência, resposta a diversas intervenções, evolução da doença, comparar os resultados com outros países, e auxiliar no planejamento de políticas públicas com implicações na saúde, nos aspectos social e econômico. O presente estudo contribui para que os profissionais de saúde no Brasil possam utilizar este instrumento para estabelecer estratégias centradas nas necessidades reais dos pacientes, uma vez que é de fácil aplicação e de fácil entendimento pelo paciente.

Os resultados desta pesquisa sobre a avaliação da fadiga e qualidade de vida relacionada à saúde em mulheres com câncer de mama submetidas à quimioterapia no Instituto Nacional de Câncer possibilitou obter informações para se poder intervir na melhora da qualidade de vida dessas mulheres e sobretudo nos cuidados e monitoramento da fadiga. Isso possibilitará aos profissionais de saúde prevenir, minimizar, reduzir e tratar os efeitos colaterais de curto e longo prazo,

decorrentes dos tratamentos neoadjuvante e adjuvante que influenciam nas atividades diárias, e assim definir em qual período as estratégias de intervenções no tratamento devem ser realizadas, principalmente em relação à necessidade de reabilitação. Este questionário de avaliação de fadiga e da qualidade de vida pode ser incorporado na prática diária dos profissionais de saúde, permitindo uma avaliação global do paciente e a identificação de suas necessidades.

É necessário dar informações ao paciente e aos cuidadores sobre a fadiga desde o começo do tratamento, com relação às opções de controle da fadiga, e orientar quanto à importância de informar aos profissionais de saúde sobre os sintomas (Cella et al., 1998). A equipe para intervenção da fadiga deve incluir médicos, enfermeiros, fisioterapeutas, terapeutas ocupacionais, nutricionistas e psicólogos (Dillon e Kelly, 2003).

A fadiga é multifatorial e as estratégias para gerenciar a fadiga envolvem modalidades combinadas. A intervenção para fadiga inclui as ações farmacológicas com agentes hematopoiéticos (*epoetin alfa ou darbepoetin alfa*) psicoestimulantes, corticosteróide e antidepressivos (Carroll et al., 2007). As intervenções não farmacológicas incluem educação do paciente, conservação de energia, modificar padrões de atividade e sono, exercícios físicos, intervenção psicológica, terapia cognitiva, adequada nutrição e hidratação (Portenoy e Itri, 1999; Berger, 2003).

Atualmente existem dados insuficientes para recomendar qualquer tipo específico de terapia complementar e alternativa para a fadiga relacionada ao câncer. Entretanto as terapias complementares e alternativas como a

acupuntura e a massagem devem ser estudadas em ensaios clínicos aleatórios (Sood et al., 2007).

Portanto, o FACT-F é um instrumento que permitirá sua aplicação em outros estudos brasileiros, possibilitando comparações dos resultados de avaliações e intervenções com outros estudos realizados, inclusive de outros países. Entretanto, é importante lembrar que, por se tratar de instrumento cujos autores detêm direitos autorais, deve ser solicitada autorização prévia à sua utilização.

5. Conclusões

O instrumento FACT-F apresentou uma boa reprodutibilidade teste-reteste em uma série heterogênea de pacientes, com diferentes tipos de câncer, *performance status* e estadiamento.

A versão na língua portuguesa do FACT-F apresentou uma alta consistência interna, bem como a validade convergente e discriminante para avaliar a fadiga e qualidade de vida em pacientes com câncer.

As mulheres com câncer de mama em quimioterapia apresentaram uma diminuição significativa nas médias dos escores do FACT-F, FACT-G e na subescala fadiga e bem-estar físico após o terceiro ciclo de quimioterapia quando comparado com os escores antes do início da quimioterapia, e a diminuição da fadiga e qualidade de vida permanece como um platô até após o 6º ciclo de quimioterapia. A fadiga está relacionada a menor qualidade de vida relacionada à saúde. A subescala fadiga em fumantes diminuiu significativamente comparada com os escores antes e depois de 6 ciclos de quimioterapia. Os escores do FACT-G antes e depois da quimioterapia em

pacientes ativos e muito ativos são maiores em comparação com pacientes sedentários e insuficientemente ativos (embora não tenha havido significância estatística). A fadiga aumentou significativamente nos pacientes sedentários e insuficientemente ativos, mais do que nos pacientes ativos e muito ativos.

Portanto, o FACT-F é um instrumento válido e confiável para avaliar a QV e fadiga, e permitirá que seja aplicado em outros estudos brasileiros possibilitando comparações dos resultados de avaliações e intervenções com outros estudos realizados inclusive de outros países. Entretanto, é importante lembrar que, por se tratar de instrumento cujos autores detêm direitos autorais, deve ser solicitada autorização prévia à sua utilização.

6. Referências Bibliográficas

Ahlberg K, Ekman T, Gaston-Johansson F, Mock V. Assessment and management of cancer-related fatigue in adults. Lancet 2003; 362:640–50.

Arnold BJ, Eremenco E, Chang CH, Odom L, Ribaudo JM, Cella D. Development of a single portuguese language version of the functional assessment of cancer therapy general (FACT G) scale. Qual Life Res 2000; 9(3): 316.

Arnold BJ, Eremenco E, Chang CH, Cella DF, Ribeiro JLP, Doro MP, *et al.* How much is “very much”? Developing a rating scale for portuguese speaking countries. Qual Life Res 2001; 10(3): 264.

Berger, A. Treating fatigue in cancer patients. Oncologist 2003; 8 (suppl 1):10-4.

Bland JM, Altman DG. Measurement in medicine: the analysis of method comparison studies. Statistician 1983; 32:307-17.

Bland, J. M. Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986; 8476(1):307-10.

Cella D. The FACT- anemia Scale. A new tool for the assessment of outcomes in cancer anemia and fatigue. Semin Hematol 1997; 34(3):13-9.

Cella D, Bonomi AE, Lloyd SR, Tulsky DS, Kaplan E, Bonomi P, et al Reliability and validity of the Functional Assessment of Cancer Therapy-Lung (FACT-L) quality of life instrument. Lung Cancer 1995; 12: 199-220.

Cella D; Mowinski CJ. Measuring quality of life in chronic illness: the funtional assessment of chronic illness therapy measurement system. Arch Phys Med Rehabil 2002; 83(suppl 2):s10-s17.

Cella D, Peterman A, Passik S*, Jacobsen P, Breitbart W.* Progress toward guidelines for the management of fatigue. Oncology *(*Huntingt) 1998; 12 (11A)*:*369- 77.

Cella D, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, et al. The functional assessment of cancer therapy scale: development and validation of the general measure. J Clin Oncol 1993; 11: 570-9.

Carroll JK, Kohli S, Mustian KM, Roscoe JA, Morrow GR. Pharmacologic treatment of cancer-related fatigue. Oncologist 2007; 12:43-51.

Cho HJ, Costa E, Menezes PR, Chalder T, Bhugra D, Wessely S. Cross-cultural validation of the Chalder Fatigue Questionnaire in Brazilian primary care. J Psychosom Res 2007; 62(3):301-4.

Colton T. Statistics in medicine. Boston: Little, Brown and Company, 1974, 211 p.

Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: cardiopulmonary and quality of life outcomes. J Clin Oncol 2003; 21:1660-8.

Curt GA. Impact of fatigue on quality of life in oncology patients. Semin Hematol 2000; 37 (Suppl 6):14-7.

Dillon E, Kelly J. The status of cancer fatigue on the Island of Ireland: AIFC professional and interim patient surveys. Oncologist 2003; 8(Suppl 1): 22–6.

Dimeo F, Schwartz S, Wesel N, Voigt A, Thiel E. Effects of an endurance and resistance exercise program on persistent cancer-related fatigue after treatment. Ann Oncol 2008; 19(8):1495-9.

Downie FP, Mar Fan HG, Houédé-Tchen N, Yi Q, Tannock IF. Cognitive function, fatigue, and menopausal symptoms in breast cancer patients receiving adjuvant chemotherapy: evaluation with patient interview after formal assessment. Psychooncology 2006; 15(10):921-30.

Esper P, Mo F, Chodak G, et al. Measuring Quality of life in men with prostate cancer using the Functional Assessment of Cancer Therapy-Prostate (FACT-P) instrument. Urology 1997; 50(6), 920-8.

Eton DT, Cella D, Yost KJ, Yount SE, Peterman AH, Neuberg DS, et al. A combination of distribution and anchor based approaches determined minimally important differences (MIDS) for four endpoints en a breast cancer scale. J Clin Epidemiol 2004; 57: 898-910.

Flechtner H, Bottomley A. Fatigue and quality of life: lessons from the real world. The Oncologist 2003; 8: Suppl 1, 5–9.

Gregory SA. Efficacy of darbepoetin alfa in the treatment of chemotherapy-Induced anemia in non-hodgkin's lymphoma. Support Cancer Ther 2006; 3(4):232-9.

Godino C, Jodar L, Durán A, Martínez I, Schiaffino A. Nursing education as an intervention to decrease fatigue perception in oncology patients. Eur J Oncol Nurs 2006; 10(2):150-5.

Hopkins WG. Measures of reliability in sports medicine and science. Sports Med, 2000; 30(1):1-15.

INCA. Instituto Nacional de Câncer. Estimativas 2008: Incidência de Câncer no Brasil. Rio de Janeiro: INCA; 2007.

Ishikawa NM, Derchain SFM; Thuler LCS. Fadiga em pacientes com câncer de mama em tratamento adjuvante. Rev Bras Cancerol 2005; 51(4): 313-8.

Lachin JM. Introduction to sample size determination and power analysis for clinical trials. Contr Clin Trials 1981; 2:93-113.

Lent L, Hahn E, Eremenco S, Webster K, Cella D. Using cross-cultural input to adapt the Functional Assessment of Chronic Illness Therapy (FACIT) scales. Acta Oncol 1999; 38(6):695-702.

Minton O, Stone P. A systematic review of the scales used for the measurement of cancer-related fatigue (CRF). Ann Oncol 2008; Aug doi:10.1093/annonc/mdn537.

Mota DD, Pimenta CA, Piper BF. Fatigue in Brazilian cancer patients, caregivers, and nursing students: a psychometric validation study of the Piper Fatigue Scale-Revised. Support Care Cancer 2008; DOI 10.1007/s00520-008-0518-x.

Mundfrom DJ, Shaw DG, Ke TL. Minimum sample size recommendations for conducting factor analyses. International Journal of Testing 2005; 5(2): 159–68.

NCI.National Cancer Institute. Fatigue (PDQ®). Disponível em: http://www.cancer.gov/cancertopics/pdq/supportivecare/fatigue/healthprofessional/page2, 30/10/2008.

Portenoy RK, Itri LM. Cancer-related fatigue: guidelines for evaluation and management. Oncologist 1999; 4(1):1-10.

Prieto, AJ. A method for translation of instruments to other languages. Adult Education Quaterly 1992; 43(1): 1-14.

Prue G, Rankin J, Allen J, Gracey J, Cramp F. Cancer-related fatigue: A critical appraisal. Eur J Cancer 2006; 42:846–63.

Scientific Advisory Committee of the Medical Outcomes Trust (Aaronson N, Alonso J, Burnam A, Lohr KN, Patrick DL, Perrin E, Stein REK). Assessing health status and quality-of-life instruments: attributes and review criteria. Qual Life Res 2002; 11: 193-205.

Segal RJ, Reid RD, Courneya KS, Malone SC, Parliament MB, Scott CG, et al. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. J Clin Oncol 2003*;* 21(9):1653-9.

Servaes P, Verhagen S, Bleijenber G. Determinants of chronic fatigue in disease-free breast cancer patients: a cross-sectional study. Ann Oncol 2002;13(4):589-98.

Sood A, Barton DL, Bauer BA, Loprinzi CL. A critical review of complementary therapies for cancer-related fatigue. Integr Cancer Ther 2007; 6(1):8-13.

Stone PC, Minton O. Cancer-related fatigue. Eur J Cancer 2008; doi:10.1016/j.ejca.2008.02.037.

Stone P, Ream E, Richardson A, Thomas H, Andrews P, Campbell P, et al. Cancer-related fatigue - a difference of opinion? Results of a multicentre survey of healthcare professionals, patients and caregivers. Eur J Cancer Care 2003; 12(1): 20-7.

Szklo M, Nieto FJ. Epidemiology: beyond the basics. Maryland: Aspen Publishers, 2000, p. 495.

Tsang KL, Carlson LE, Olson K. Pilot crossover trial of Reiki versus rest for treating cancer-related fatigue. Integr Cancer Ther 2007; 6(1):25-35.

Vadhan-Raj S, Mirtsching B, Charu V, Terry D, Rossi G, Tomita D, et al. Assessment of hematologic effects and fatigue in cancer patients with chemotherapy-induced anemia given darbepoetin alfa every two weeks. J Support Oncol 2003; 1(2):131-8.

Visser MR, Smets EM. Fatigue, depression and quality of life in cancer patients: how are they related? Support Care Cancer 1998; 6(2):101-8.

Yellen SB, Cella DF, Webster K, Blendowski C, Kaplan E. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. J Pain Symptom Manage 1997; 13(2):63-74.

Wadler S, Brain C, Catalano P, Einzig AI, Cella D, Benson AB 3rd. Randomized phase II trial of either fluorouracil, parenteral hydroxyurea, interferon-alpha-2a, and filgrastim or doxorubicin/docetaxel in patients with advanced gastric cancer with quality-of-life assessment: eastern cooperative oncology group study E6296. Cancer J 2002; 8(3): 282-6.

Ward WL, Hahn EA, Mo F, Hernandez L, Tulsky DS, Cella D. Reliability and validity of the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) quality of life instrument. Qual Life Res 1999; 8(3):181-95.

Webster K, Cella D, Yost K. The functional assessment of chronic illness therapy measurement system: properties, applications, and interpretation. Health Qual Life Outcomes 2003; 1:79.

Webster K, Odom L, Peterman A, Lent L, Cella D. The functional assessment of chronic illness therapy (FACIT) measurement system: validation of version 4 of the core questionnaire. Qual Life Res 1999; (7): 604.

Weitzner MA, Meyers CA, Gelke C, Byrne K, Cella D, Levin VA. The Functional Assessment of Cancer Therapy (FACT) scale: Development of a brain subscale and revalidation of the general version (FACT-G) in patients with primary brain tumors. Cancer 1995; 75(5), 1151-61.

Wratten C, Kilmurray J, Nash S, Seldon M, Hamilton CS, O'Brien PC, et al. Fatigue during breast radiotherapy and its relationship to biological factors. Int J Radiat Oncol Biol Phys 2004; 59(1):160-7.

7. Anexos

7.1. Anexo 1 – Metodo

Primeiramente foi avaliada a reprodutibilidade do questionário Functional *Assessment of Cancer Therapy-Fatigue* (FACT-F) através do teste-reteste para a língua portuguesa em pacientes com câncer.

O estudo foi prospectivo. O tamanho da amostra para este tipo de estudo é de pelo menos 50 sujeitos (Scientific Advisory Committee of the Medical Outcomes Trust, 2002; Hopkins, 2000), que é o mínimo recomendado para estudos de reprodutibilidade teste-reteste. Foram incluídos 85 pacientes neste estudo de reprodutibilidade teste-reteste. A reprodutibilidade das informações dos questionários, no presente estudo, foi analisada por meio de dois procedimentos estatísticos: coeficiente de correlação intraclasse (CCI) entre os valores obtidos nas duas medidas (teste-reteste) e diagrama de dispersão proposto por Bland-Altman, no qual foram comparadas graficamente as diferenças entre os valores obtidos no teste e no reteste do FACT-F ($FACTF_{teste}$ – $FACTF_{reteste}$) com as médias das duas avaliações [($FACTF_{teste}$ + $FACTF_{reteste}$) /2]. Como limite de concordância no

diagrama de Bland-Altman, considerou-se duas vezes o desvio-padrão da média das diferenças entre os resultados (Bland e Altman, 1983; Bland e Altman, 1986). Além disso, foi calculado o coeficiente de correlação de Pearson, visando a comparar os resultados obtidos com os do artigo original de validação do FACT-F para a língua inglesa. Os coeficientes de correlação de Pearson foram classificados como: 0-0,25 não correlacionado; 0,25-0,50 correlação fraca; 0,50-0,75 correlação moderada a boa; >0,75 correlação muito boa a excelente (Colton, 1974). O CCI pode variar de 0 a +1, neste caso indicando uma alta reprodutibilidade, enquanto CCI=0 indica nenhuma reprodutibilidade (Szklo e Nieto, 2000).

Para a validação do questionário foram incluídos mais 185 pacientes além dos 85 pacientes do teste-reteste, assim totalizando 270 sujeitos em tratamento quimioterápico por câncer. O tamanho mínimo da amostra sugerida para estabelecer a validade de uma escala é de 3 a 20 vezes o número de variáveis do instrumento (Mundfrom et al., 2005). A confiabilidade foi avaliada pela consistência interna e reprodutibilidade. A validade convergente foi analisada através da correlação entre o FACT-F e SF-36. A validade discriminante da FACT-F avaliou a habilidade da escala em discriminar pacientes segundo a ECOG *Performance Status*, e diferentes estádios da doença.

Após a validação, o questionário foi utilizado no estudo para avaliar a fadiga e qualidade de vida em mulheres com câncer de mama estádios II e III que foram indicadas para receber no mínimo seis ciclos de quimioterapia neoadjuvante ou adjuvante com fluoracil, adriamicina, ciclofosfamida. O FACT-F foi aplicado antes da quimioterapia e após terceiro e sexto ciclo de quimioterapia.

Para o cálculo do tamanho da amostra, partiu-se do pressuposto de que a diferença mínima estimada a ser encontrada para o escore de fadiga antes da quimioterapia e após quimioterapia seria de 3 (Cella, et al., 2002; Webster et al., 2003), obtendo-se tamanho mínimo da amostra para identificar essa diferença que foi de 127 mulheres, considerando um erro tipo ? de 0,05 e erro tipo ? de 0,20 (Lachin, 1981). Para avaliar a qualidade de vida das mulheres com câncer de mama, partindo do pressuposto de que a diferença mínima estimada encontrada para o escore de qualidade de vida antes da quimioterapia e após quimioterapia seria de 5 (Webster et al., 2003; Eton et al., 2004), o tamanho mínimo da amostra para identificar essa diferença foi de 143 mulheres, considerando um erro ? de 0,05 e erro ? de 0,20 (Lachin, 1981). Portanto, a amostra para avaliar fadiga e qualidade de vida em mulheres antes da quimioterapia e após a quimioterapia para este estudo foi de 143 mulheres.

O teste de Wilcoxon foi realizado para avaliar as diferenças entre antes do início do ciclo, e após terceiro e sexto ciclos de quimioterapia, e para comparar grupos de pacientes entre a quimioterapia neoadjuvante *versus* adjuvante. O coeficiente de correlação de Pearson foi utilizado para analisar a relação entre a subescala fadiga e o escore do FACT-G total e nos diferentes domínios. O pacote estatístico Statistical Package for the Social Sciences (SPSS) versão 13.0 foi utilizado para todas as análises estatísticas.

7.2. Anexo 2 – Carta de Autorização do FACT

De: "Helen Morrow" <hmorrow@facit.org>
Para: <nelimuraki@globo.com>
Assunto: Re: Re: Brazilian validation FACT F
Data: Tue, 1 Mar 2005 08:55:02 –0600
Anexos: *FACT-G_v4_por_final_30May01.doc* [**abrir**]
FACT-G_v4_por_final_30May01.doc [**abrir**]
FACT-G_v4_por_final_30May01.doc [**abrir**]
FACT-G_v4_por_final_30May01.doc [**abrir**]
FACT-G_v4_por_final_30May01.doc [**abrir**]
FACT-G_v4_por_final_30May01.pdf [**abrir**]
ScoringFACT-G v4-REVISED.doc [**abrir**]
Administration Guidelines.doc [**abrir**]
FACIT-F_POR_Final_Ver4_28Nov01.pdf [**abrir**]
FACIT-F_POR_Final_Ver4_28Nov01.doc [**abrir**]
ScoringFACIT-F v4-REVISED.doc [**abrir**]

Hello Neli Muraki Ishikawa:
Thank you for completing the Translation Request form. After reviewing your request, and speaking with Ben Arnold, Manager of the Translation Project, he has granted you permission to use the FACT-G and FACIT-F in Portuguese (as originally requested) for this study only, waiving the standard licensing fee normally associated with the use of translated questionnaires. I have attached a copy of the most current version of the FACT-G and FACIT-F questionnaire (Version 4) in Portuguese for your review and possible use. With your agreement to a few simple requests, we ask that you review our user's agreement that can be found on our website at www.facit.org (See Requests & Registration: User's Agreement). Should you actually decide to include the questionnaire in your research, we would also request that you take the time to complete a Collaborator's Project Information Form on line to submit for our files. We are in the process of updating our website, so, many areas of the site are under construction. We appreciate your patience as we continue to create an efficient and user friendly site.

Please keep in mind that the questionnaire has a copyright attached and can not be altered without strict permission from Ben Arnold. I have attached the scoring and administration guidelines as well as the raw scoring template for the FACT-G and FACIT-F. The raw scoring templates will eventually be available on our new website; however, a fee will be associated with this downloadable form. These documents are only available in English. During this transition, we will not be charging a fee.

I hope you will find this information useful. If you have additional questions, please do not hesitate to contact me again.

Thank you,
Helen A. Morrow, MA
Manager, Business Operations
www.facit.org
hmorrow@facit.org

7.3. Anexo 3 – Parecer do Comitê de Ética em Pesquisa do INCA

MINISTÉRIO DA SAÚDE
Instituto Nacional de Câncer
Comitê de Ética em Pesquisa-INCA

Memo. 083/05-CEP-INCA

Rio de Janeiro, 11 de agosto de 2005

A: Dra. Neli Muraki Ishikawa
Pesquisadora Principal

Ref.: Prot. 61/05 – Avaliação da fadiga e qualidade de vida em mulheres com câncer de mama em quimioterapia

Prezada Doutora,

Informamos que o Comitê de Ética em Pesquisa do Instituto Nacional de Câncer após re-análise **aprovou** o Protocolo intitulado: Avaliação da fadiga e qualidade de vida em mulheres com câncer de mama em quimioterapia, bem como seu Termo de Consentimento Livre e Esclarecido (versão agosto de 2005) em 08 de agosto de 2005.

2. Estamos encaminhando a documentação pertinente para o CONEP, com vistas a registro e arquivamento.

Atenciosamente,

Dra. Adriana Scheliga
Coordenadora do Comitê de Ética em Pesquisa
CEP-INCA

7.4. Anexo 4 –Termo de Consentimento Livre e Esclarecido (Validação do questionário FACT-F)

MINISTÉRIO DA SAÚDE
Instituto Nacional de Câncer
Comitê de Ética em Pesquisa-INCA
Aprovação CEP 08/08/05

Termo de Consentimento Livre e Esclarecido para validação dos questionários

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Pesquisa: Avaliação da fadiga e qualidade de vida em pacientes com câncer em quimioterapia.

Pesquisadora principal: **Neli Muraki Ishikawa**, Fisioterapeuta do INCA

Tel. Trabalho (21) 3970-7884, 3970-7945

Nome da Paciente: _____

Matrícula: ☐☐☐☐☐☐☐ Idade: ☐☐

Endereço: _____

Bairro: _____ Cidade:_____

CEP: ☐☐☐☐☐-☐☐☐ **Telefone**: ☐☐☐☐☐☐☐☐

Código: ☐☐☐

Você está sendo convidada a participar como voluntário, de um estudo que faz parte da tese de doutorado da fisioterapeuta Neli Muraki Ishikawa, do Instituto Nacional de Câncer, na Universidade Estadual de Campinas (UNICAMP) sobre a avaliação de fadiga e qualidade de vida em pacientes com câncer tratadas com quimioterapia.

A pesquisa tem como objetivo estudar a fadiga e a qualidade de vida em um grupo de pacientes com câncer em tratamento de quimioterapia atendidos no INCA. O teor dessas perguntas é relacionado a questões pessoais, e será perguntado sobre seu bem estar físico, social/familiar, emocional e funcional.

Caso você aceite participar desta pesquisa, responderá a um questionário de qualidade de vida para pessoas com câncer chamado FACT-G, um questionário de qualidade de vida chamado SF 36 e um questionário de fadiga FACIT-F, após 3 a 7 dias você responderá novamente o questionário FACT-G e FACIT-F. Se houver necessidade, terá ajuda do pesquisador, que poderá apenas ler as perguntas, para, então, respondê-las.

Dra. Adriana Scheliga
Coordenadora
Comitê de Ética em Pesquisa
CEP - INCA

O tempo gasto nas respostas aos três questionários não será superior a 20 minutos e você precisará apenas marcar as opções que melhor corresponderem ao seu entendimento das perguntas formuladas.

Você não será beneficiado diretamente com os resultados . Os benefícios esperados após a conclusão do estudo será trazer melhor qualidade de vida para mulheres com câncer de mama prevenindo, minimizando e reduzindo os efeitos colaterais de curto e longo prazo decorrentes da fadiga.

A presente pesquisa não oferece riscos e a sua participação nesse estudo é VOLUNTÁRIA, e você tem o direito de desistir e interromper a sua participação a qualquer momento, sem necessidade de justificar esta decisão, e isto não terá nenhuma conseqüência no seu atendimento no INCA. O investigador principal poderá retirá-lo do estudo caso seja observado violação dos critérios de sua inclusão no estudo.

A sua identificação será mantida como informação confidencial. Os resultados serão publicados e/ou divulgados em eventos científicos, sem a revelação de sua identidade.

Nenhum tipo de remuneração ou compensação será fornecido pelo Ministério da Saúde/INCA, pela sua participação na pesquisa, bem como não haverá nenhum custo adicional para você, pois não haverá marcação especial de atendimento para participar dessa pesquisa, já que se respeitará a marcação de consulta ambulatorial.

Você pode fazer perguntas a qualquer momento. Se você tiver problema ou tenha mais questões a respeito de seleção, do estudo ou de seus direitos na qualidade de paciente, por favor procure ou ligue para o Dra. Adriana Scheliga Coordenadora do Comitê de Ética em Pesquisa do INCA na Rua André Cavalcanti 37 – 2° andar - telefone: (21) 3233-1410.

Responda às perguntas a seguir, circulando SIM ou NÃO

5. Você leu e entendeu este TERMO DE CONSENTIMENTO? SIM NÃO
6. Todas as suas dúvidas sobre este estudo foram esclarecidas? SIM NÃO
7. Você entendeu que seus dados pessoais serão examinados pelos investigadores participantes deste estudo? SIM NÃO
8. Você concorda em ser incluído neste estudo? SIM NÃO

Receberei uma cópia assinada e datada deste Consentimento informado. Não renuncio a

Dra. Adriana Scheliga
Coordenadora
Comitê de Ética em Pesquisa
CEP - INCA

nenhum de meus direitos legais ao assinar o presente formulário de Consentimento.

Nome do paciente (letra de forma): _____

Assinatura do paciente : _____

Idade: _____ Data: _____/_____/_____.

Nome do representante legal (letra de forma): _____

Assinatura do representante : _____

Data: _____/_____/_____.

Testemunha 1 (letra de forma): _____

Assinatura:_____

Data: _____/_____/_____.

Eu, abaixo assinado expliquei todos os detalhes relevantes deste estudo para o paciente identificado acima e/ou representante legal e darei uma cópia assinada e datada deste documento.

Nome do Investigador/ Co-investigador:_____

Assinatura do Investigador/ Co-investigador:_____

Data: _____/_____/_____.

Dra. Adriana Scheliga
Coordenadora
Comitê de Ética em Pesquisa
CEP - INCA

7.5. Anexo 5 –Termo de Consentimento Livre e Esclarecido (Avaliação da fadiga e qualidade de vida em mulheres com câncer de mama)

MINISTÉRIO DA SAÚDE
Instituto Nacional de Câncer
Comitê de Ética em Pesquisa-INCA
Aprovação CEP 08/08/05

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Pesquisa: Avaliação da fadiga e qualidade de vida em mulheres com câncer de mama em quimioterapia.

Pesquisadora principal: **Neli Muraki Ishikawa**, Fisioterapeuta do INCA

Tel. Trabalho (21) 3970-7884, 3970-7945

Nome da Paciente: _____

Matrícula: ☐☐☐☐☐☐☐ Idade: ☐☐

Endereço: _____

Bairro: _____ Cidade: _____

CEP: ☐☐☐☐☐-☐☐☐ **Telefone**: ☐☐☐☐☐☐☐☐

Código: ☐☐☐

Você está sendo convidada a participar como voluntária, de um estudo que faz parte da tese de doutorado da fisioterapeuta Neli Muraki Ishikawa, do Instituto Nacional de Câncer na Universidade Estadual de Campinas (UNICAMP) sobre a avaliação de fadiga e qualidade de vida em mulheres com câncer tratadas com quimioterapia.

A pesquisa tem como objetivo estudar a fadiga e a qualidade de vida em um grupo de mulheres portadoras de câncer de mama, atendidas no INCA, antes da quimioterapia e após o 3° e 6° ciclo de quimioterapia. O teor dessas perguntas é relacionado a questões pessoais, e será perguntado sobre seu bem estar físico, social/familiar, emocional e funcional.

Caso você aceite participar desta pesquisa, responderá a um questionário de qualidade de vida e um questionário de fadiga antes da quimioterapia e após o 3° e 6° ciclo de quimioterapia.. Se houver necessidade, terá ajuda do pesquisador, que poderá apenas ler as perguntas, para, então, respondê-las.

O tempo gasto nas respostas aos dois questionários não será superior a 15 minutos e você precisará apenas marcar as opções que melhor corresponderem ao seu entendimento das perguntas formuladas.

Dra. Adriana Scheliga
Coordenadora
Comitê de Ética em Pesquisa
CEP - INCA

Você não será beneficiada diretamente com os resultados . Os benefícios esperados após a conclusão do estudo será trazer melhor qualidade de vida para mulheres com câncer de mama, prevenindo, minimizando e reduzindo os efeitos colaterais de curto e longo prazo decorrentes da fadiga.

A presente pesquisa não oferece riscos e a sua participação nesse estudo é VOLUNTÁRIA, e você tem o direito de desistir e interromper a sua participação a qualquer momento, sem necessidade de justificar esta decisão, e isto não terá nenhuma conseqüência no seu atendimento no INCA. O investigador principal poderá retirá-la do estudo caso seja observada violação dos critérios de sua inclusão no estudo.

A sua identificação será mantida como informação confidencial. Os resultados serão publicados e/ou divulgados em eventos científicos, sem a revelação de sua identidade.

Nenhum tipo de remuneração ou compensação será fornecido pelo Ministério da Saúde/INCA, pela sua participação na pesquisa, bem como não haverá nenhum custo adicional para você, pois não haverá marcação especial de atendimento para participar dessa pesquisa, já que se respeitará a marcação de consulta ambulatorial.

Você pode fazer perguntas a qualquer momento. Se você tiver problema ou tenha mais questões a respeito de seleção, do estudo ou de seus direitos na qualidade de paciente, por favor procure ou ligue para o Dra. Adriana Scheliga Coordenadora do Comitê de Ética em Pesquisa do INCA na Rua André Cavalcanti 37 – 2° andar - telefone: (21) 3233-1410.

Responda às perguntas a seguir, circulando SIM ou NÃO

1. Você leu e entendeu este TERMO DE CONSENTIMENTO? SIM NÃO
2. Todas as suas dúvidas sobre este estudo foram esclarecidas? SIM NÃO
3. Você entendeu que seus dados pessoais serão examinados pelos investigadores participantes deste estudo? SIM NÃO
4. Você concorda em ser incluído neste estudo? SIM NÃO

Receberei uma cópia assinada e datada deste Consentimento informado. Não renuncio a nenhum de meus direitos legais ao assinar o presente formulário de Consentimento.

Dra. Adriana Scheliga
Coordenadora
Comitê de Ética em Pesquisa
CEP - INCA

Nome do paciente (letra de forma): _____

Assinatura do paciente : _____

Idade: _____ Data: ____/____/____.

Nome do representante legal (letra de forma): _____

Assinatura do representante : _____

Data: ____/____/____.

Testemunha 1 (letra de forma): _____

Assinatura: _____

Data: ____/____/____.

Eu, abaixo assinado expliquei todos os detalhes relevantes deste estudo para o paciente identificado acima e/ou representante legal e darei uma cópia assinada e datada deste documento.

Nome do Investigador/ Co-investigador: _____

Assinatura do Investigador/ Co-investigador: _____

Data: ____/____/____.

Dra. Adriana Scheliga
Coordenadora
Comitê de Ética em Pesquisa
CEP - INCA

7.6. Anexo 6 – Características Sociodemográficas (Validação do FACT-F)

Data: _____/_____/_____ número: I__I__I__I

Nome: _____

Telefone:_____ matricula: I__I__I__I__I__I__I__I

Data: _____/_____/_____ número: I__I__I__I

DADOS SOCIODEMOGRÁFICOS

- Idade: I__I__I anos
- Sexo: I__I masculino I__I feminino
- Estado civil: I__I casada I__I desquitada ou separada I__I divorciada
  I__I viúva I__I solteira
- Cor: I__I branca I__I preta I__I amarela I__I parda I__I indígena
- Escolaridade: I__I alfabetização de adultos I__I antigo primário
  I__I antigo ginásio I__I antigo clássico ou científico
  I__I ensino fundamental ou 1° grau
  I__I ensino médio ou 2° grau superior mestrado ou doutorado I__I nenhum
- Fumante (mais de 100 cigarros): I__I sim I__I não
  I__I Fumante atual I__I Ex fumante
- Atividade física: I__I sedentário I__I insuficientemente ativo
  I__I muito ativo I__I ativo

CARACTERÍSTICAS DA DOENÇA

Câncer (tipo):_____

Estádio: I__I 0 I__I I I__I II I__I III I__I III I__I IV

Performance Status: I__I 0 I__I 1 I__I 2 I__I 3 I__I 4

Cirurgia: I__I sim I__I não

Radioterapia: I__I sim I__I não

Quimioterapia: I__I adjuvante I__I neoadjuvante I__I recidiva/paliativa

Hormonioterapia: I__I sim I__I não

Índice de massa corporal: I__I__I,I__I Peso I__I__I__I,I__I Kg Altura I__I,I__I__I m

I__I abaixo do peso (<18,5) I__I peso ideal (18,5-24,9)

I__I pré obesidade (25-29,9) I__I obesidade I (30-34,9)

I__I obesidade II (35-39,9) I__I obesidade III (= 40)

7.7. Anexo 7 – Características Sociodemográficas (Avaliação de fadiga e qualidade de vida em mulheres com câncer de mama)

Data: _____/_____/_____ número: I__I__I__I

Nome: _____

Telefone:_____ matricula: I__I__I__I__I__I__I__I

Data: _____/_____/_____ número: I__I__I__I

DADOS SOCIODEMOGRÁFICOS

- Idade: I__I__I anos
- Sexo: I__I masculino I__I feminino
- Estado civil: I__I casada I__I desquitada ou separada I__I divorciada
  I__I viúva I__I solteira
- Cor: I__I branca I__I preta I__I amarela I__I parda I__I indígena
- Escolaridade: I__I alfabetização de adultos I__I antigo primário
  I__I antigo ginásio I__I antigo clássico ou científico
  I__I ensino fundamental ou 1° grau
  I__I ensino médio ou 2° grau superior mestrado ou doutorado I__I nenhum
- Fumante (mais de 100 cigarros): I__I sim I__I não
  I__I Fumante atual I__I Ex fumante
- Atividade física: I__I sedentário I__I insuficientemente ativo
  I__I muito ativo I__I ativo

CARACTERÍSTICAS DA DOENÇA

Estádio: I__I 0 I__I I I__I II A I__I II B I__I III A I__I III B I__I IV

Cirurgia: I__I tumorectomia/quadrantectomia I__I mastectomia simples ou total
I__I mastectomia radical modificada I__I mastectomia radical
I__I mastectomia com reconstrução imediata

- Antes do 1° ciclo de quimioterapia Data: _____/_____/_____

Performance Status: I__I 0 I__I 1 I__I 2 I__I 3 I__I 4

Índice de massa corporal: I__I__I,I__I Peso I__I__I__I,I__I Kg Altura I__I,I__I__I m
I__I abaixo do peso (<18,5) I__I peso ideal (18,5-24,9)
I__I pré obesidade (25-29,9) I__I obesidade I (30-34,9)
I__I obesidade II (35-39,9) I__I obesidade III (= 40)

• Depois do 3° ciclo de quimioterapia Data: _____/_____/_____

Performance Status: I__I 0 I__I 1 I__I 2 I__I 3 I__I 4

Índice de massa corporal: I__I__I,I__I Peso I__I__I__I,I__I Kg Altura I__I,I__I__I m

I__I abaixo do peso (<18,5) I__I peso ideal (18,5-24,9)

I__I pré obesidade (25-29,9) I__I obesidade I (30-34,9)

I__I obesidade II (35-39,9) I__I obesidade III (= 40)

• Depois do 6° ciclo de quimioterapia Data: _____/_____/_____

Performance Status: I__I 0 I__I 1 I__I 2 I__I 3 I__I 4

Índice de massa corporal: I__I__I,I__I Peso I__I__I__I,I__I Kg Altura I__I,I__I__I m

I__I abaixo do peso (<18,5) I__I peso ideal (18,5-24,9)

I__I pré obesidade (25-29,9) I__I obesidade I (30-34,9)

I__I obesidade II (35-39,9) I__I obesidade III (= 40)

7.8. Anexo 8 – FACT- F Versão 4

Abaixo encontrará uma lista de afirmações que outras pessoas com a sua doença disseram ser importantes. **Por favor, faça um círculo em torno do número que melhor corresponda ao seu estado durante os últimos 7 dias**.

	BEM-ESTAR FÍSICO	**Nem um pouco**	**Um pouco**	**Mais ou menos**	**Muito**	**Muitíssimo**
GP1	Estou sem energia	0	1	2	3	4
GP2	Fico enjoado (a)	0	1	2	3	4
GP3	Por causa do meu estado físico, tenho dificuldade em atender às necessidades da minha família	0	1	2	3	4
GP4	Tenho dores	0	1	2	3	4
GP5	Sinto-me incomodado (a) pelos efeitos secundários do tratamento	0	1	2	3	4
GP6	Sinto-me doente	0	1	2	3	4
GP7	Tenho que me deitar durante o dia	0	1	2	3	4
	BEM-ESTAR SOCIAL/FAMILIAR	**Nem um pouco**	**Um pouco**	**Mais ou menos**	**Muito**	**Muitíssimo**
GS1	Sinto que tenho uma boa relação com os meus amigos	0	1	2	3	4
GS2	Recebo apoio emocional da minha família	0	1	2	3	4
GS3	Recebo apoio dos meus amigos	0	1	2	3	4
GS4	A minha família aceita a minha doença	0	1	2	3	4
GS5	Estou satisfeito (a) com a maneira como a minha família fala sobre a minha doença	0	1	2	3	4
GS6	Sinto-me próximo (a) do(a) meu (minha) parceiro(a) (ou da pessoa que me dá maior apoio)	0	1	2	3	4
Q1	*Independentemente do seu nível atual de atividade sexual, favor responder à pergunta a seguir. Se preferir não responder, assinale o quadrículo [ ] e passe para a próxima seção*					
GS7	Estou satisfeito (a) com a minha vida sexual	0	1	2	3	4

FACT-Fatigue (Versão 4)

Por favor, faça um círculo em torno do número que melhor corresponda ao seu estado durante os últimos 7 dias

	BEM-ESTAR EMOCIONAL	Nem um pouco	Um pouco	Mais ou menos	Muito	Muitís-simo
GE1	Sinto-me triste	0	1	2	3	4
GE2	Estou satisfeito (a) com a maneira como enfrento a minha doença.	0	1	2	3	4
GE3	Estou perdendo a esperança na luta contra a minha doença	0	1	2	3	4
GE4	Sinto-me nervoso (a)	0	1	2	3	4
GE5	Estou preocupado (a) com a idéia de morrer	0	1	2	3	4
GE6	Estou preocupado (a) que o meu estado venha a piorar	0	1	2	3	4

	BEM-ESTAR FUNCIONAL	Nem um pouco	Um pouco	Mais ou menos	Muito	Muitís-simo
GF1	Sou capaz de trabalhar (inclusive em casa)	0	1	2	3	4
GF2	Sinto-me realizado (a) com o meu trabalho (inclusive em casa)	0	1	2	3	4
GF3	Sou capaz de sentir prazer em viver	0	1	2	3	4
GF4	Aceito a minha doença	0	1	2	3	4
GF5	Durmo bem	0	1	2	3	4
GF6	Gosto das coisas que normalmente faço para me divertir	0	1	2	3	4
GF7	Estou satisfeito (a) com a qualidade da minha vida neste momento	0	1	2	3	4

FACT-Fatigue (Versão 4)

Por favor, faça um círculo em torno do número que melhor corresponda ao seu estado durante os últimos 7 dias

	PREOCUPAÇÕES ADICIONAIS	Nem um pouco	Um pouco	Mais ou menos	Muito	Muitíssimo
HI 7	Sinto-me fatigado (a)	0	1	2	3	4
HI 12	Sinto fraqueza generalizada	0	1	2	3	4
An 1	Sinto-me sem forças	0	1	2	3	4
An 2	Sinto-me cansado (a)	0	1	2	3	4
An 3	Tenho dificuldade em começar as coisas porque estou cansado (a)	0	1	2	3	4
An 4	Tenho dificuldade em acabar as coisas porque estou cansado(a)	0	1	2	3	4
An 5	Tenho energia	0	1	2	3	4
An 7	Sou capaz de fazer as minhas atividades normais	0	1	2	3	4
An 8	Preciso (de) dormir durante o dia	0	1	2	3	4
An 12	Estou cansado (a) demais para comer	0	1	2	3	4
An 14	Preciso de ajuda para fazer as minhas atividades normais	0	1	2	3	4
An 15	Estou frustrado (a) por estar cansado (a) demais para fazer as coisas que quero	0	1	2	3	4
An 16	Tenho que limitar as minhas atividades sociais por estar cansado (a)	0	1	2	3	4

7.9. Anexo 9 – FACIT-F Scoring Guidelines (Version 4) Pages 1

Instructions:* 1. Record answers in "item response" column. If missing, mark with an X
2. Perform reversals as indicated, and sum individual items to obtain a score.
3. Multiply the sum of the item scores by the number of items in the subscale, then divide by the number of items answered. This produces the subscale score.
4. Add subscale scores to derive total scores (TOI, FACT-G & FACIT-F).
5. **The higher the score, the better the QOL.**

Subscale	Item Code	Reverse item?		Item response	Item Score
PHYSICAL WELL-BEING (PWB)	GP1	4	-	_____	=_____
	GP2	4	-	_____	=_____
	GP3	4	-	_____	=_____
	GP4	4	-	_____	=_____
Score range: 0-28	GP5	4	-	_____	=_____
	GP6	4	-	_____	=_____
	GP7	4	-	_____	=_____
				Sum individual item scores: _____	
				Multiply by 7: _____	
				Divide by number of items answered: _____= **PWB subscale score**	
SOCIAL/FAMILY WELL-BEING (SWB)	GS1	0	+	_____	=_____
	GS2	0	+	_____	=_____
	GS3	0	+	_____	=_____
	GS4	0	+	_____	=_____
Score range: 0-28	GS5	0	+	_____	=_____
	GS6	0	+	_____	=_____
	GS7	0	+	_____	=_____
				Sum individual item scores: _____	
				Multiply by 7: _____	
				Divide by number of items answered: _____= **SWB subscale score**	
EMOTIONAL WELL-BEING (FWB)	GE1	4	-	_____	=_____
	GE2	0	+	_____	=_____
	GE3	0	-	_____	=_____
	GE4	0	-	_____	=_____
Score range: 0-24	GE5	0	-	_____	=_____
	GE6	0	-	_____	=_____
				Sum individual item scores: _____	
				Multiply by 6: _____	
				Divide by number of items answered: _____=**EWB subscale score**	
FUNCTIONAL WELL-BEING (FWB)	GF1	0	+	_____	=_____
	GF2	0	+	_____	=_____
	GF3	0	+	_____	=_____
	GF4	0	+	_____	=_____
Score range: 0-28	GF5	0	+	_____	=_____
	GF6	0	+	_____	=_____
	GF7	0	+	_____	=_____
				Sum individual item scores: _____	
				Multiply by 7: _____	
				Divide by number of items answered: _____=**FWB subscale score**	

FACIT-F Scoring Guidelines (Version 4) – Page 2

Subscale Score	Item Code	Reverse item?		Item response	Item
FATIGUE	HI7	4	-	_____	=_____
SUBSCALE	HI12	4	-	_____	=_____
(FS)	An1	4	-	_____	=_____
	An2	4	-	_____	=_____
Score range: 0-52	An3	4	-	_____	=_____
	An4	4	-	_____	=_____
	An5	0	+	_____	=_____
	An7	0	+	_____	=_____
	An8	4	-	_____	=_____
	An12	4	-	_____	=_____
	An14	4	-	_____	=_____
	An15	4	-	_____	=_____
	An16	4	-	_____	=_____

Sum individual item scores: _____
Multiply by 13: _____
Divide by number of items answered: _____ **=F Subscale score**

To Derive a FACT-G total score:
Score range: 0-108

_____ + _____ + _____ +_____ = **FACT-G Total score**
(**PWB** score) (**SWB** score) (**EWB** score) (**FWB** score)

To Derive a FACIT-F total score:
Score range: 0-160

_____ + _____ + _____ + _____=_____=**FACT-F Total score**
(**PWB** score) (**SWB** score) (**EWB** score) (**FWB** score) (**FS** score)

*For guidelines on handling missing data and scoring options, please refer to the Administration and Scoring Guidelines in the manual or on-line at www.facit.org

7.10. Anexo 10 – Questionário de Qualidade de Vida SF-36

Instruções: esta pesquisa questiona você sobre sua saúde. Estas informações nos manterão informados de como você se sente e quão bem você é capaz de realizar suas atividades de vida diária. Responda cada questão marcando a resposta como indicado. Caso você esteja inseguro de como responder, tente fazer melhor que puder.

1. Em geral, você diria que sua saúde é:
   Excelente (1)
   Muito boa (2)
   Boa (3)
   Ruim (4)
   Muito ruim (5)

2. Comparada a um ano atrás, como você classificaria sua saúde em geral, agora?
   Muito melhor agora do que um ano atrás (1)
   Um pouco melhor agora do que um ano atrás (2)
   Quase a mesma de um ano atrás (3)
   Um pouco pior agora do que um ano atrás (4)
   Muito pior agora do que um ano atrás (5)

3. Os seguintes itens são sobre atividades que você poderia fazer atualmente durante um dia comum. Devido à sua saúde, você tem dificuldade para fazer estas atividades? Neste caso, quanto?

Atividades	**Sim, dificulta muito**	**Sim dificulta pouco**	**Não, não dificulta de modo algum**
A. atividades vigorosas, que exigem muito esforço, tais como correr, levantar objetos pesados, participar de esportes árduos...	1	2	3
B. atividades moderadas, tais como mover urna mesa, passar aspirador de pó, jogar bola, varrer a casa...	1	2	3
C. levantar ou carregar mantimentos	1	2	3
D. subir vários lances de escadas	1	2	3
E. subir um lance de escada	1	2	3
F. curvar-se, ajoelhar-se ou dobrar-se	1	2	3
G. andar mais que um quilômetro	1	2	3
H. andar vários quarteirões	1	2	3
I. andar um quarteirão	1	2	3
J. tomar banho ou vestir-se	1	2	3

4. Durante as últimas 4 semanas você teve algum dos seguintes problemas com o seu trabalho ou com alguma atividade diária regular, como conseqüência de sua saúde física?

	Sim	Não
A Você diminuiu a quantidade de tempo que dedicava ao seu trabalho ou a outras atividades?	1	2
B. Realizou menos tarefas do que gostaria?	1	2
C. Esteve limitado no seu tipo de trabalho ou em outras atividades?	1	2
D. Teve dificuldade de fazer seu trabalho ou outras atividades (p. ex. necessitou de um esforço extra)?	1	2

5. Durante as últimas 4 semanas você teve algum dos seguintes problemas com o seu trabalho ou outra atividade regular diária, como conseqüência de algum problema emocional (como sentir-se deprimido ou ansioso)?

	Sim	Não
A. Você diminuiu a quantidade de tempo que dedicava ao seu trabalho ou a outras atividades?	1	2
B. Realizou menos do que você gostaria?	1	2
C. Não trabalhou ou não fez qualquer atividade com tanto cuidado como geralmente faz?	1	2

6. Durante as últimas 4 semanas de que maneira sua saúde física ou problemas emocionais interferiram nas suas atividades sociais normais, em relação à família, vizinhos, amigos ou em grupo?
   - De forma nenhuma (1)
   - Ligeiramente (2)
   - Moderadamente (3)
   - Bastante (4)
   - Extremamente (5)

7. Quanta dor no corpo você teve durante as últimas quatro semanas?
   - Nenhuma (1)
   - Muito leve (2)
   - Leve (3)
   - Moderada (4)
   - Grave (5)
   - Muito Grave (6)

8. Durante as últimas 4 semanas quanto a dor interferiu em seu trabalho normal (incluindo tanto o trabalho fora como dentro de casa)?
   - De maneira nenhuma (1)
   - Um pouco (2)
   - Moderadamente (3)
   - Bastante (4)
   - Extremamente (5)

9. Estas questões são como você se sente, e como tudo tem acontecido com você durante as últimas 4 semanas. Para cada questão dê uma resposta que mais se aproxime da maneira como você se sente.

	Todo tempo	A maior parte do tempo	Uma boa parte do tempo	Alguma parte do tempo	Uma pequena parte do tempo	Nunca
A. Quanto tempo você tem se sentido cheio de vigor, cheio de vontade, cheio de força?	1	2	3	4	5	6
B. Quanto tempo você tem se sentido uma pessoa muito nervosa?	1	2	3	4	5	6
C. Quanto tempo você tem se sentido tão deprimido que nada possa animá-lo?	1	2	3	4	5	6
D.Quanto tempo você tem se sentido calmo ou tranqüilo?	1	2	3	4	5	6
E. Quanto tempo você tem se sentido com muita energia?	1	2	3	4	5	6
F. Quanto tempo você tem se sentido desanimado e abatido?	1	2	3	4	5	6
G Quanto tempo você tem se sentido esgotado?	1	2	3	4	5	6
H. Quanto tempo você tem se sentido uma pessoa feliz?	1	2	3	4	5	6
I. Quanto tempo você tem se sentido cansado?	1	2	3	4	5	6

10. Durante as últimas 4 semanas, quanto de seu tempo a sua saúde física ou problemas emocionais interferiram em suas atividades sociais (como visitar amigos, parentes, etc.)?

Todo o tempo	(1)
A maior parte do tempo	(2)
Alguma parte do tempo	(3)
Uma pequena parte do tempo	(4)
Nenhuma parte do tempo	(5)

11. O quanto verdadeiro ou falso é cada uma das afirmações para você?

	Definitiva-mente verdadeiro	A maioria das vezes verdadeiro	Não sei	A maioria das vezes falsa	Definitiva mente falsa
A. Eu costumo adoecer um pouco mais facilmente que as outras pessoas	1	2	3	4	5
B. Eu sou tão saudável quanto qualquer pessoa que conheço	1	2	3	4	5
C.Eu acho que minha saúde vai piorar	1	2	3	4	5
D. Minha saúde é excelente	1	2	3	4	5