

Pre-operative fatigue in cancer patients: prevalence and associated factors

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ABSTRACT

This study aimed to describe the prevalence of fatigue and to identify factors associated with fatigue in patients in the pre-operative phase for oncologic surgery. We conducted a cross-sectional study with 117 pre-operative cancer patients (mean age = 51.2 years; 76.9% women; 65.8% lived with a partner; 70.9% did not have previous cancer treatment). We used the instruments Piper Fatigue Scale-Revised; Perceived Stress Scale; Hospital Anxiety and Depression Scale; Pain Numerical Scale; Numerical Sleep Scale and Karnofsky Performance Status Scale. We conducted Chi-Square test, Student's t-test, and one-way ANOVA. We found a 25.6% prevalence of pre-operative fatigue and the intensity was moderate/severe. The affective fatigue dimension presented higher score compared to behavioral and sensorial/psychological dimensions. Anxiety, depression, stress, pain, sleep and performance status were associated with pre-operative fatigue.

Descriptors: Fatigue; Neoplasms; Surgical Procedures, Operative; Perioperative Nursing.

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INTRODUCTION

Fatigue of the surgical patient is still understudied, and data about this theme during the pre-operative phase are incipient⁽¹⁻²⁾. Fatigued patients in the pre-operative phase tend to be more fatigued in the post-operative phase and, consequently, they can have a slower post-operative recovery, extending the hospitalization period, increasing the risk of hospital infection, affecting the continuation of the anti-cancer treatment and, delaying the start of adjuvant therapies⁽¹⁻³⁾. Thus, to assess this symptom during pre-operative phase becomes useful to plan individualized interventions, such as planning the activity/rest cycle, nutritional guidance, and management of possible causal factors as depression or anemia⁽⁴⁾.

Fatigue is a subjective, multi-dimensional and, multi-factorial symptom. It is an unpleasant physical sensation, with cognitive and emotional symptoms described as tiredness, and that is not relieved with the application of usual energy restoration and preservation strategies⁽⁵⁾. Fatigued patients express feelings of tiredness, incapacity to keep the usual routine, loss of libido, verbalization of a constant lack of energy, within among others⁽⁶⁾.

Pre-operative fatigue is rarely an isolated symptom, more commonly occurring in association with other symptoms. In an integrative review describing the evolution of perioperative fatigue in cancer patients and its associated factors, the pre-operative fatigue was frequently associated with anxiety and depression. It also allowed us to observe that its intensity tended to increase in patients submitted to neoadjuvant chemotherapy or radiotherapy, reaching a moderate level⁽⁷⁻⁹⁾.

There is a research need referring to fatigue in oncologic patients submitted to surgery, once the pre-operative fatigue is an experience with a significant negative repercussion. We noted a lack of knowledge about this multi-dimensional experience in Brazil, about the related factors to its occurrence and intensity, harming the planning of more effective actions for prevention and treatment of the symptom by health professionals. Being aware of this, we developed the present study to describe the prevalence of fatigue and to identify the associated factors to the presence of fatigue in oncologic patients in the pre-operative period.

METHODS

We conducted an analytical cross-sectional study with a convenience sample of 117 adult individuals with an indication for conventional and elective oncologic surgery, from April 2014 to January 2015. We performed this study in two large hospital institutions in Goiânia, Goiás, Brazil.

The inclusion criteria were: to be 18 years or older, to have indication for medium or large surgery as a cancer treatment with curative or palliative purpose; to present ASA I or ASA II for surgical risk assessment, according to the classification of the American Society of Anesthesiologist (ASA); to not have had previous surgery for at least two months prior to the current one; to be able to read and write; and to have compensated comorbidities.

Instruments

We used the Piper Fatigue Scale-Revised (PIPER) to assess fatigue⁽¹⁰⁻¹¹⁾. It is a multi-dimensional instrument with 22 items distributed in three dimensions. The physical behavioral dimension evaluates functional capacity

components that can be affected by fatigue. The affective dimension tries to identify the interpretation or meaning given to fatigue. The sensorial/psychological dimension gathers the self-perception, emotional and cognitive components. Each item is presented in a numerical scale (0 to 10), and the total score and the dimensions' scores are represented from zero to 10, with the higher scores representing higher fatigue level. We considered the patients fatigued when presenting scores different from zero in the PIPER scale an, based in the total score; we classified fatigue as light (score <4), moderate (score ≥ 4 and <7) and severe (score ≥ 7).

We used the Perceived Stress Scale (PSS) to assess stress perception. Fourteen questions compose the scale and they verify how unpredictable, uncontrollable and overloaded the respondents evaluate their lives. Each item has answering options varying from zero to four, being zero equal to never and four, always. The scale total ranges from zero and 56, and the higher the score, the higher the stress. This instrument is validated for use in Brazil⁽¹²⁾.

We used the Hospital Anxiety and Depression Scale (HADS) to identify signs and symptoms commonly related to anxiety and depression. Fourteen items compose the instrument, being seven for anxiety and seven for depression assessment. Each item grades from zero to three and, the scores are calculated independently for each disorder, varying from zero to 21. For this study, we adopted a cut-point ≥ 9 . This instrument is validated for use in Brazil with patients submitted to surgery⁽¹³⁾.

We used the Pain Numerical Scale to measure pain intensity. It is a scale presented in a horizontal line, with 100mm of extension, with anchors in the extremities: 0 (zero) = no pain and 10 (ten) = worse imaginable pain. We used the Sleep Numerical Scale to assess sleep impairment. It is presented in a horizontal line, with 100mm of extension, with anchors in the extremities: 0 (zero) = no sleep impairment and 10 (ten) = totally impaired sleep. We used the Karnofsky Performance Status Scale (KPS) to assess the level of functional compromise⁽¹⁴⁾. Its score varies from 100% indicating full health to 0%, meaning death. It is a broadly used instrument in Brazilian medicine, used to assess the patient's capacity in conduct activities of the daily life and the need for hospitalization considering the signs and symptoms of the disease. The instrument is also used to compare the functionality in patients receiving different therapies, including to help establish prognosis.

Additionally, we analyzed clinical data as smoking, comorbidities, antineoplastic neoadjuvant treatments and previous surgeries.

Data collection process

This study is part of research entitled "Perioperative fatigue: comparison between patients with and without cancer", approved by the Ethics in Research Committees of the institutions involved, protocol nº 532.145 and 608.861-0.

We recruited the participants during visits of nurses and trained nursing students to the hospitalization units searching for patients admitted for surgical treatment. We invited patients meeting the inclusion criteria to participate in the study, 36 to two hours before the surgery. They signed the Informed Consent Term after reading it and clarifying questions. They filled the instruments through the interview, clinical examination, and consultation of the medical record.

Data analysis

We analyzed the data using the statistical program SPSS (Statistical Package for Social Science), and we adopted a 5% significance level. We described the categorical variables as absolute and relative frequencies, and the continuous variables as means, standard deviations, minimum and maximum values. To verify data normality, we used the Kolmogorov-Smirnov test. We applied the Person's Chi-Square (X^2) and likelihood ratio tests to explore the association between categorical variables. We used the Student's t-test and Mann-Whitney test to compare continuous variables of patients with and without fatigue. The one-way ANOVA assessed if the mean scores of the PIPER scale's dimensions were equal.

RESULTS

Sociodemographic characteristics

The mean age was 51.2 years, 44 (37.6%) patients had up to six years of education, and 60 (51.3%) reported per capita income lower than one current minimum wage salary. Most patients were female ($n=90$; 76.9%), lived with a partner ($n=77$; 65.8%), had brown skin color ($n=68$; 58.1%), were not smokers ($n=105$; 89.7%) and did not perform previous cancer treatment ($n=83$; 70.9%). There was no significant difference between fatigue and the sociodemographic characteristics (Table 1).

Table 1: Distribution of patients with and without fatigue according to sociodemographic and clinical characteristics. Goiânia, GO, Brazil, 2014-2015.

Variables	With Fatigue		Without Fatigue		p
	(n=30)		(n=87)		
	n	%	n	%	
Age					
Mean(SD); min-max	49.1 (14.8); 21.0-88.0		51.9 (15.0); 18.0-87.0		0.740 ^c
Income per capita					
Mean(SD); min-max	582.2 (249.8); 233.3-1250		653.9(312.7); 140-3000		0.987 ^d
Education (years)					
Mean(SD); min-max	8.9;(3.8); 1.0; 16.0		8.4(4.1); 1.0; 16.0		0.851 ^d
Sex:					
Female	26	86.7	64	73.6	0.125 ^a
Male	4	13.3	23	26.4	
With partner					
Yes	17	56.7	60	69.0	0.221 ^b
No	13	43.3	27	31.0	
Skin color:					
White	11	36.7	28	32.2	0.721 ^a
Black	2	6.7	6	6.9	
Brown	17	56.7	51	58.6	
Indigenous	-		2	2.3	
Smoking					
Not smoker	26	86.7	79	90.8	0.535 ^a
Ex-smoker	0	0.0	1	1.1	
Smoker	4	13.3	7	8.0	
Had surgery					
Yes	4	13.3	19	21.8	0.284 ^a
No	26	86.7	67	77.0	
Neo chemotherapy					
Yes	3	10.0	16	18.4	0.262 ^a
No	27	90.0	71	81.6	
Neo radiotherapy					
Yes	1	3.3	9	10.3	0.196 ^a
No	29	96.7	78	89.7	

^a likelihood ratio test; ^b Pearson's Chi-Square; ^c Student's t-test for independent samples; ^d Mann-Whitney's test; * Some data were left in blank by participants, and for this reason, the sum does not reach the total (100%).

Fatigue

The fatigue prevalence among patients in pre-operative phase for oncologic surgery was 25.6% (n=30), of those 15.3% (n=18) presented severe, 9.4% (n=11) moderate, and 0.9% (n=1), light fatigue.

From the assessment of the PIPER scale's dimensions, the mean score of the affective fatigue was significantly higher than the mean scores of the behavioral, and the sensorial/cognitive/emotional dimensions (Table 2).

Table 2: Fatigue intensity according to Piper Scale (n=30). Goiânia, GO, Brazil, 2015.

	Behavioral dimension	Affective dimension	Sensorial/psychological dimension
Mean (SD)	6.3 (2.2)	8.1 (1.4)*	5.6 (1.6)
Min - Max	1.8 - 10.0	5.4 - 10.0	1.8 - 9.6
CI** 95%	5.4 - 7.1	7.6 - 8.6	5.0 - 6.2

One-way ANOVA; * p<0.05; **CI= Confidence interval.

The results of association tests between fatigue and clinical variables showed fatigue significantly associated with anxiety, depression, stress, pain, sleep and performance status (Table 3).

Table 3: Association between fatigue (PIPER scale) and the variables anxiety, depression, stress, pain, sleep, and performance status. Goiânia, GO, Brazil, 2015.

Instruments		With fatigue	Without fatigue	p
		n (%)	n (%)	
HADS A	With anxiety	20 (66.7)	45 (51.7)	0.006
	Without anxiety	10 (33.3)	42 (48.3)	
HADS D	With depression	17 (56.7)	21 (24.1)	0.004
	Without depression	13 (43.3)	66 (75.9)	
PSS	High stress perception	27 (90.0)	60 (69.0)	0.015
	Low stress perception	3 (10.0)	27 (31.0)	
Pain	With pain	23 (76.7)	44 (50.6)	0.004
	Without pain	6 (20.0)	44 (50.6)	
Sleep	With impairment	26 (86.7)	51 (58.6)	<0.001
	Without impairment	6 (20.0)	44 (50.6)	
KPS	100% - 90%	10 (33.3)	71 (81.6)	<0.001
	≤ 80%	20 (66.7)	15 (17.2)	

HADS A: Hospital Anxiety and Depression Scale - Anxiety; HADS D: Hospital Anxiety and Depression Scale – Depression; PSS: Perceived Stress Scale; KPS: Karnofsky Performance Status.

DISCUSSION

Sociodemographic characteristics

The results did not demonstrate an association between fatigue and the sociodemographic variables. On the one hand, these results corroborate with findings of other authors, reinforcing the hypothesis that the pre-operative fatigue is not associated to sex, age, to live with a partner, skin color and, income per capita⁽¹⁵⁾. On the other hand, a few studies present different results. Women with breast cancer during the pre-operative phase had fatigue associated with education and to have a partner⁽¹⁶⁾. Another study, also involving women with breast cancer during pre-operative phase identified the association between fatigue and marital status, age, children, employment⁽¹⁷⁾, that is, women with low educational levels, single, older, with children and no job, had more pre-operative fatigue.

Although many articles point the association between fatigue and chemotherapy, radiotherapy and smoking^(7,18), our results did not show such association. The same was seen in other studies showing that

neoadjuvant chemotherapy did not influence the severity of symptoms, proving that neoadjuvant anti-neoplastic therapies did not predict fatigue⁽¹⁹⁻²⁰⁾.

Pre-operative fatigue

The results indicated the prevalence of pre-operative fatigue equal to 25.6%. Few studies also found a similar prevalence. Research with colorectal cancer patients of both sexes found fatigue reported by 22% of patients before surgery⁽²¹⁾. Patients with prostate cancer had fatigue prevalence of 14.3%; in patients with breast cancer, it was 20.3%; and, in patients with cancers in the gastrointestinal tract, fatigue was referred by 28.1% of interviewed patients⁽²²⁾.

Of the patients fatigued in the pre-operative phase, the vast majority referred moderate to severe fatigue. This result indicated that fatigue of these surgical patients is clinically significant, demanding measures for its control. When examining the literature, it was seen that few studies presented results similar to ours and that patients had moderate fatigue before the surgical treatment^(8-9,23). Those studies were conducted with patients of both sexes, with a mean age of 58 years, during the pre-operative period for cancer in the high digestive tract, lung, breast and, gynecological. A study assessed patients with bone or soft tissue cancer and found a prevalence of 29.7%, and from those, 35% had severe fatigue before surgery⁽³⁾.

Regarding the domains of the Fatigue Scale, the affective dimension obtained the highest mean score. Noting the perception regarding the symptoms during the wait before surgery can be more evident and be interpreted as negative, making the fatigue more unpleasant, unacceptable, destroyer and abnormal, once in most times, this situation was never experimented by the patient⁽¹⁰⁾. We found only one study that reported the fatigue dimension, and it was conducted with women with breast cancer, and the domains with the highest score were the physical, followed by affective and cognitive⁽²⁰⁾. The affective dimension was not the one with the highest score in this case, but it had a significant presence, confirming its loss to the patient, as found in our study. Although the studies referred the importance of multi-dimensional instruments, few are assessing the fatigue dimension, hindering the comparison of results.

Frequently, the patient in the pre-operative phase, recently diagnosed with cancer, has not been submitted to other sources causing fatigue, besides cancer itself, emotions caused by the diagnosis and by the expectation of the surgical procedure. In the present study, all clinical factors assessed (anxiety, depression, stress, pain, sleep, and performance) were associated with fatigue. Similar results were previously described, where the impact of these factors seem to intensify the fatigue manifestation^(3,24). Being indispensable that, especially in these patients, professionals should investigate and assess fatigue, in a way to avoid it to be under-diagnosed and under-treated, causing more considerable losses in the patient's recovery⁽³⁾.

Nowadays, many publications report a cluster of symptoms including fatigue^(18,25). Future studies with larger samples will be able to confirm the results found in the present study and, also, to search clusters of symptoms for patients in pre-operative phase of oncologic surgery.

CONCLUSIONS AND IMPLICATIONS FOR RESEARCH AND CLINICAL PRACTICE

This study suggests a significant percentage of cancer patients, in the pre-operative phase, presenting clinically significant fatigue, considering the symptom intensity. Fatigue prevalence between pre-operative patients for oncologic surgery was 25.6%. The affective dimension of fatigue presented significantly higher scores than other dimensions and, knowing this; the professional should act in the interpretation of the symptom referred by patients, for example, guiding their coping focusing in the problem and not on the emotions.

The results of this study showed an association between pre-operative fatigue and anxiety, depression, stress and sleep changes. In a particular way, these symptoms are expected and considered normal in people who are close to being submitted to surgery. Because there are expectations that these symptoms are present, unfortunately, when present, they are not adequately assessed and managed. Other factors like pain and worsening in functionality, are also associated to fatigue. It is likely for these two factors to be related to cancer, and not to the expectation of the surgical procedure, although it is known that pain is also multi-dimensional and influenced by emotions.

Nursing assistance to the patient in pre-operative phase is a challenge. The nurse, together with the multi-professional team can help by detecting these symptoms, especially fatigue, through valid and reliable instruments. Fatigue identification and its assessment using a multi-dimensional instrument provide evidence to define interventions for fatigue.

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REFERENCES

1. Schroeder D, Hill GL. Predicting postoperative fatigue: importance of preoperative factors. *World J Surg* [Internet]. 1993 [cited 2018 sep 05];17(2):226-31. Available from: <https://doi.org/10.1007/BF01658931>.
2. Gorini MIPC, Silva POS, Chaves PL, Ercole JP, Cardoso BC. Registro do diagnóstico de enfermagem fadiga em prontuários de pacientes oncológicos. *Acta paul. enferm.* [Internet]. 2010 [cited 2018 sep 05]; 23(3):356-8. Available from: <https://doi.org/10.1590/S0103-21002010000300007>.
3. Van der Geest ICM, Knoop H, Veth RPH, Schreuder HWB, Bleijenberg G. High fatigue scores before and after surgical treatment of bone and soft tissue tumors. *Exp Ther Med* [Internet]. 2013 [cited 2018 sep 05];5(1):205-8. Available from: <https://doi.org/10.3892/etm.2012.786>.
4. Bulechek GM, Butcher HK, Dochterman JM, Wagner CM. *Nursing Interventions Classification (NIC)*. 6th ed. St Louis: Elsevier-Mosby; 2013.
5. Mota DDCF, Cruz DALM, Pimenta CAM. Fadiga: uma análise do conceito. *Acta paul. enferm.* [Internet]. 2005 [cited 2018 sep 05];18(3):285-93. Available from: <https://doi.org/10.1590/S0103-21002005000300009>.
6. Herdman TH. *Diagnósticos de enfermagem da NANDA: definições e classificação 2012-2014*. Porto Alegre: ARTMED; 2013.
7. Oliveira MM, Oliveira GF, Souza-Talarico JN, Mota DDCF. Surgical Oncology: Evolution of Postoperative Fatigue and Factors Related to Its Severity. *Clin J Oncol Nurs* [Internet]. 2016 [cited 2018 sep 05];20(1):E-3-8. Available from: <https://doi.org/10.1188/16.CJON.E3-E8>.
8. Barbour AP, Lagergren P, Hughes R, Alderson D, Barham CP, Blazeby JM. Health-related quality of life among patients with adenocarcinoma of the gastro-oesophageal junction treated by gastrectomy or oesophagectomy. *Br J Surg* [Internet]. 2008 [cited 2018 sep 05];95(1):80-4. Available from: <https://doi.org/10.1002/bjs.5912>.
9. Schrepf A, Clevenger L, Christensen D, DeGeest K, Bender D, Ahmed A, et al. Cortisol and inflammatory processes in ovarian cancer patients following primary treatment: relationships with depression, fatigue, and disability. *Brain Behav Immun* [Internet]. 2013 [cited 2018 sep 05];30 Suppl:S126-34. Available from: <https://doi.org/10.1016/j.bbi.2012.07.022>.
10. Piper BF, Dibble SL, Dodd MJ, Weiss MC, Slaughter RE, Paul SM. The revised Piper Fatigue Scale: psychometric evaluation in women with breast cancer. *Oncol Nurs Forum*. 1998 May;25(4):677-84.

11. Mota DDCF, Pimenta CAM, Piper BF. Fatigue in Brazilian cancer patients, caregivers and nursing students: a psychometric validation study of the Piper Fatigue Scale-Revised. *Support Care Cancer* [Internet]. 2009 [cited 2018 sep 05];17(6):645-52. Available from: <https://doi.org/10.1007/s00520-008-0518-x>.
 12. Luft CB, Sanches SO, Mazo GZ, Andrade A. Versão brasileira da escala de estresse percebido: tradução e validação para idosos. *Rev Saude Publica* [Internet]. 2007 [cited 2018 sep 05];41(4):606-615. Available from: <https://doi.org/10.1590/S0034-89102007000400015>.
- Retratado
13. Marcolino JAM, Mathias LAST, Piccinini Filho L, Guaratini AA, Suzuki FM, Alli LAC. Escala Hospitalar de Ansiedade e Depressão: Estudo da validade de critério e da confiabilidade com pacientes no pré-operatório. *Rev Bras Anestesiol* [Internet]. 2007 [cited 2018 sep 05];57(1):52-62. Available from: <http://www.scielo.br/pdf/%0D/rba/v57n1/06.pdf>.
 14. Karnofsky DA, Burchenal JH. The Clinical Evaluation of Chemotherapeutic Agents. In: MacLeod CM, editor. *Evaluation of Chemotherapeutic Agents*. New York: Columbia Univ. Press; 1949. p. 196.
 15. Lockefer JP, De Vries J. What is the relationship between trait anxiety and depressive symptoms, fatigue, and low sleep quality following breast cancer surgery? *Psychooncology* [Internet]. 2013 [cited 2018 sep 05];22(5):1127-33. Available from: <https://doi.org/10.1002/pon.3115>.
 16. Huang HP, Chen ML, Liang J, Miaskowski C. Changes in and predictors of severity of fatigue in women with breast cancer: A longitudinal study. *Int J Nurs Stud* [Internet]. 2014 [cited 2018 sep 05];51(4):582-92. Available from: <https://doi.org/10.1016/j.ijnurstu.2013.09.003>.
 17. Michielsen HJ, Van der Steeg AFW, Roukema JA, De Vries J. Personality and fatigue in patients with benign or malignant breast disease. *Support Care Cancer* [Internet]. 2007 [cited 2018 sep 05];15(9):1067-73. Available from: <https://doi.org/10.1007/s00520-007-0222-2>.
 18. Thomas BC, Waller A, Malhi RL, Fung T, Carlson LE, Groff SL, et al. A longitudinal analysis of symptom clusters in cancer patients and their sociodemographic predictors. *J Pain Symptom Manage* [Internet]. 2014 [cited 2018 sep 05];47(3):566-78. Available from: <https://doi.org/10.1016/j.jpainsymman.2013.04.007>.
 19. Sarna L, Cooley ME, Brown JK, Chernecky C, Elashoff D, Kotlerman J. Symptom severity 1 to 4 months after thoracotomy for lung cancer. *Am J Crit Care* [Internet]. 2008 [cited 2018 sep 05];17(5):455-67. Available from: <http://ajcc.aacnjournals.org/content/17/5/455.long>.
 20. Haghighat S, Akbari ME, Holakouei K, Rahimi A, Montazeri A. Factors predicting fatigue in breast cancer patients. *Support Care Cancer* [Internet]. 2003 [cited 2018 sep 05];11(8):533-8. Available from: <https://doi.org/10.1007/s00520-003-0473-5>.
 21. Tsunoda A, Nakao K, Tsunoda Y, Watanabe M, Matsui N. Health-related quality of life of colorectal cancer patients receiving oral UFT plus leucovorin compared with those with surgery alone. *Int J Clin Oncol* [Internet]. 2010 [cited 2018 sep 05];15(2):153-60. Available from: <https://doi.org/10.1007/s10147-010-0035-z>.
 22. Goedendorp MM, Gielissen MFM, Verhagen CAH, Peters MEJW, Bleijenberg G. Severe fatigue and related factors in cancer patients before the initiation of treatment. *Br J Cancer* [Internet]. 2008 [cited 2018 sep 05];99(9):1408-14. Available from: <https://doi.org/10.1038/sj.bjc.6604739>.
 23. Montgomery GH, Schnur JB, Erblich J, Diefenbach MA, Bovbjerg DH. Presurgery psychological factors predict pain, nausea, and fatigue one week after breast cancer surgery. *J Pain Symptom Manage* [Internet]. 2010 [cited 2018 sep 05];39(6):1043-52. Available from: <https://doi.org/10.1016/j.jpainsymman.2009.11.318>.
 24. Denieffe S, Cowman S, Gooney M. Symptoms, clusters and quality of life prior to surgery for breast cancer. *J Clin Nurs* [Internet]. 2014 [cited 2018 sep 05];23(17-18):2491-502. Available from: <https://doi.org/10.1111/jocn.12430>.
 25. Trudel-Fitzgerald C, Savard J, Ivers H. Longitudinal changes in clusters of cancer patients over an 18-month period. *Health Psychol* [Internet]. 2014 [cited 2018 sep 05];33(9):1012-22. Available from: <https://doi.org/10.1037/a0033497>.