RESEARCH COMMUNICATION

Quality of Life in Breast Cancer Patients - A Quantile Regression Analysis

Mohamad Amin Pourhoseingholi[1], Azadeh Safaee[1]*, Bijan Moghimi-Dehkordi[1], Bahram Zeighami[2], Soghrat Faghihzadeh[3], Hamid Reza Tabatabaee[1], Asma Pourhoseingholi[1]

Abstract

Background: Quality of life study has an important role in health care especially in chronic diseases, in clinical judgment and in medical resources supplying. Statistical tools like linear regression are widely used to assess the predictors of quality of life. But when the response is not normal the results are misleading. The aim of this study is to determine the predictors of quality of life in breast cancer patients, using quantile regression model and compare to linear regression. Methods: A cross-sectional study conducted on 119 breast cancer patients that admitted and treated in chemotherapy ward of Namazi hospital in Shiraz. We used QLQ-C30 questionnaire to assessment quality of life in these patients. A quantile regression was employed to assess the assocciated factors and the results were compared to linear regression. All analysis carried out using SAS. Results: The mean score for the global health status for breast cancer patients was 64.92±11.42. Linear regression showed that only grade of tumor, occupational status, menopausal status, financial difficulties and dyspnea were statistically significant. In spite of linear regression, financial difficulties was not significant in quantile regression analysis for and dyspnea was only significant for first quartile. Also emotion functioning and duration of disease were statistically predicted QOL's score in third quartile. Conclusion: The results have demonstrated that using quantile regression leads to better interpretation and richer inference about predictors of breast cancer patient's quality of life.

Key Words: Quality of life - Iranian breast cancer - quantile regression - linear regression - QLQ-C30

Asian Pacific J Cancer Prev, **9**, 487-490

Introduction

Quality of life (QOL) has become a part of the evaluation criteria for cancer therapy (Aaronson et al., 1988). It is a subjective concept and its definitions and the sub concepts involved have varied. Recently, it has been recognized that a more comprehensive assessment of the cancer patient is necessary and that the evaluation of outcomes must move beyond traditional biomedical endpoints to include assessments of the impact of disease and its treatment on patients' quality of life (Aaronson et al., 1993).

In a simple way, QOL is individual imaginations or thoughts from life style according to his/her objectives, expectations, standards and preferences. QOL is a multidimensional construct encompassing perceptions of both positive and negative aspects of dimensions such as physical, emotional, social and cognitive functions , as well as the negative aspects of somatic discomfort and other symptoms produced by a disease or its treatment (Lehto et al., 2005).

Statistical tools such as linear regression are widely used to assess the associated factors with the quality of life. Multiple linear regression allows researchers to assess how the mean of a conditional distribution changes with respect to patient characteristics. But in most cases of interest, the biometrical measurements are not normally distributed, so parametric model such as linear regression that needs normality assumption can not informative enough (Green and Silverman, 1994). In this situation quantiles are more favorable to picture the distribution of response variable. Quantile regression (Koenker and Bassett, 1987; Koenker and Hallock, 2001) is an econometric regression model in which a specified conditional quantile (or percentile) of the outcome variable is expressed as a linear function of subject characteristics. This is in contrast to linear regression, that the mean of a continuous response is expressed as a linear function of a

*[1]Research Center of Gastroenterology and Liver Diseases, Shahid Beheshti University (M.C.), Tehran, [2]Shiraz University of Medical Sciences, Faculty of Health, Shiraz, [3]Department of Biostatistics, Tarbiat Modares University, Tehran, Iran *For correspondence: azadesafaee@yahoo.com, Aminphg@gmail.com*

set of independent or predictor variables. One of quantile regression's most appealing features is its ability to estimate quantile-specific effects that describe the impact of covariates not only on the center but on the tails of the outcome distribution. Therefore this technique is capable of providing a more complete statistical analysis of the stochastic relationships among random variables.

Not only this model frequently used in the econometrics literature (Levin, 2001; Buchinsky, 1994) but also recently in the field of biostatistics, it is used to find conditional quantile functions to provide a more complete view (Austin and Schull, 2003; Marcotte and Wilcox-Gok, 2003; Austin et al., 2005).

The aim of this study was to assess breast cancer patients' QOL and recognize the factors that affect QOL by quantile regression and compare this model to linear regression.

Patients and Methods

Quantile regression analysis:

Koenker and Bassett (1987) introduced quantile regression as a regression based method to model the quantiles of the response variable conditional on the covariates (Koenker and Bassett, 1987). Quantile regression is recently emerging as an attractive alternative to popular models (Koenker and Bassett, 1987; Koenker and Bilias, 2001; Koenker and Geling, 2001). By modeling the distribution of the response in a flexible semiparametric way, quantile regression does not impose modeling assumptions that may not be hold. This technique is intended to estimate, and conduct inference about conditional quantile functions.

In linear regression with least square technique, the coefficients are estimated so as to minimize the sum of squared deviations from the regression lines but in quantile regression, the pth quantile of the conditional distribution can be modeled as a linear function of subject characteristics. For example if someone wants to estimate median regression (Birkes and Dodge, 2003), then pth quantile is equal to 0.5 for all observations. But there is no closed-form expression to estimation and an iterative algorithm must be used to obtain the coefficient estimates (Koenker and Gilchrist, 2001). In practical works, quantile regression is similar to linear regression. Some macros have been developed in software such as SAS (PROC QUANTREG) and R (package quantreg) to fit the models of interest and researcher also can use either forward or backward model selection techniques similar to those available for multiple linear regression. Quantile regression models can include interaction terms like linear regression and the coefficients are interpreted in the same way.

Quality of life study:

A cross-sectional study conducted on 119 random samples of breast cancer patients that admitted and treated in chemotherapy ward of Namazi hospital in Shiraz city, south of Iran during Jan to Feb 2006. This center is a referral center in south of province. Any patients with a new diagnosis of breast cancer, according to pathology report, under chemotherapy were eligible to enter the study. The exclusion criteria were: cancer diagnosis less than 2 months; recurrent of breast cancer cognitive impairment; other previous or concurrent malignancies. We used QLQ-C30 questionnaire to assessment QOL in these patients. This questionnaire is a valid and reliable questionnaire for evaluation of quality of life in Iran (Safaee and Moghimi-Dehkordi, 2007).

The QLQ-C30 is multidimensional, made up of 30 items (five functional domains: physical, role, emotional, cognitive, and social, one global QOL domain, three symptom domains: fatigue, nausea-vomiting, pain, and six single items). The scores are transformed into 0–100 point scales.

Table 1. Predictors of QOL by Linear Regression Analysis

	Full Model			Final Model		
Variable	C	SE	p	C	SE	p
Physical functions	-0.12	0.13	0.37	-	-	-
Role functions	0.02	0.09	0.78	-	-	-
Emotion functions	-0.02	-0.02	0.82	-	-	-
Cognitive functions	0.22	0.10	0.03	-	-	-
Social functions	-0.22	0.12	0.07	-	-	-
Fatigue	-0.06	0.11	0.56	-	-	-
Nausea & vomiting	-0.11	0.08	0.17	-	-	-
Pain	-0.16	0.10	-0.14	-	-	-
Dyspnea	-0.16	0.08	-0.17	-0.09	0.04	0.01
Insomnia	-0.07	0.05	0.15	-	-	-
Constipation	0.01	0.08	0.89	-	-	-
Financial problems	-0.10	0.05	0.04	-0.05	0.02	0.03
Grade of tumor	-16.05	3.10	<0.001	-15.74	2.75	<0.001
Disease duration	6.71	5.56	0.23	-	-	-
Menopause	6.49	4.29	0.13	6.66	2.43	0.01
Occupation	7.64	5.50	0.16	8.86	3.19	0.01
First treatment	-7.19	5.30	0.17	-	-	-

C, coefficient, SE, standard error, p, p value

Results

Total of 119 patients with breast cancer were entered to this study. The mean age was 48.3 (SD=11.4) years. The mean score for the global health status for breast cancer patients was 64.9±11.4.

The results of the linear regression analyses showed that only grade of tumor, occupational status, menopausal status, financial difficulties and dyspnea were statistically significant for predicting patients' QOL in final model (see Table 1). Duration of disease, and other symptom scales were not significant. In spite of linear regression, financial difficulties was not significant in any quantile regression analysis for each quartile and dyspnea was only significant for first quartile. Also emotion functioning and duration of disease were statistically predicted QOL's score in third quartile. Results from quantile regression indicated that although the grade of tumor was significant in all quartiles, it predicted QOL more worth in first quartile than second and third ones. The same story was also going on for occupation, showing that the QOL's scores increased for the occupied patients in the first quartile as compared to the second and third quartiles (seeTable 2).

Table 2. Predictors of QOL by Quantile Regression Analysis

Variable	First Quartile			Second Quartile			Third Quartile		
	Coefficient	SE	p-value	Coefficient	SE	p-value	Coefficient	SE	p-value
Physical functions	-0.10	0.11	0.34	0.01	0.09	0.91	-0.02	0.10	0.83
Role functions	0.03	0.10	0.76	-0.02	0.06	0.69	0.01	0.06	0.82
Emotion functions	-0.01	0.08	0.90	0.006	0.05	0.91	0.10	0.06	0.08
Cognitive functions	0.03	0.11	0.78	0.03	0.07	0.65	0.03	0.08	0.69
Social functions	-0.02	0.10	0.79	0.001	0.09	0.98	-0.13	0.09	0.15
Fatigue	-0.02	0.07	0.73	-0.03	0.08	0.67	-0.05	0.10	0.61
Nausea & vomiting	-0.01	0.07	0.89	-0.03	0.06	0.62	0.12	0.09	0.18
Pain	-0.07	0.10	0.48	-0.02	0.09	0.83	-0.12	0.09	0.19
Dyspnea	-0.18	0.09	0.06	-0.06	0.08	0.46	0.02	0.06	0.73
Insomnia	-0.04	0.04	0.40	-0.01	0.03	0.65	-0.01	0.04	0.82
Constipation	-0.03	0.10	0.77	0.07	0.08	0.40	0.08	0.08	0.29
Financial problems	-0.07	0.04	0.10	-0.02	0.04	0.47	-0.03	0.04	0.46
Grade of tumor	-26.10	3.00	<0.001	-22.58	2.27	<0.001	-20.66	2.28	<0.001
Disease duration	0.70	2.05	0.73	0.43	1.92	0.82	4.73	2.22	0.03
Menopause	7.40	3.20	0.02	7.42	3.13	0.02	8.53	3.46	0.01
Occupation	9.79	4.57	0.03	8.32	3.42	0.01	4.26	4.55	0.35
First treatment	0.20	4.10	0.96	1.03	3.27	0.75	-1.41	4.07	0.72

Discussion

Researchers have traditionally used either OLS regression to evaluate the impact of patient characteristics on data. OLS seeks to model the mean of a random response as a function of observed explanatory factors; quantile regression seeks to model this function for each given quantile separately. By modeling the distribution of the response in a flexible semiparametric way, quantile regression does not impose modeling assumptions that may not be hold.

Although quantile regression is frequently used in econometric (Buchinsky, 1994; Koenker and Bassett, 1987; Koenker and Hallock, 2001), in the field of medicine where some data tends to concentrate on first or last quantiles researchers recently are interested in using this model. Our study has demonstrated that the use of quantile regression allows for richer inferences to be drawn a picture of impact of patient characteristics on QOL's score.

In this study both linear regression and quantile regression demonstrated consistency and strength of the relationship between grade of tumor, occupation, dyspnea, menopause status and breast cancer patients' quality of life. The strongest influence on QOL in our study was grade of tumor. Financial difficulties was significant in linear regression and emotion functioning was significant in quantile regression. During the active phase of treatment physical functioning has an enormous impact on QOL. Patients may experience acute treatment side effects in addition to cancer-related symptoms which can be emotionally distressing and debilitating. Previous studies have demonstrated the relationship between physical factors and emotional distress (Hartl et al., 2003; Avis et al., 2005; Greimel et al., 2002).

Concerning demographic factors (age, education, and marital status) the subgroups did not differ from one another. Some research, but not all, indicates that younger women may suffer poorer QOL following a breast cancer diagnosis (Brenner et al., 2005; Klee et al., 2000).

In conclusion, we have demonstrated that using quantile regression allows researchers to find the impact of patient characteristic on the time duration response. The linear regression provides at best case an incomplete picture of the association between time response and characteristic factors and leads to unreliable results in the case of severe skewness. As a result researchers should be interested in quantile regression's advantages to evaluate and provide a complete view of changing in time response distribution with patient factors and characteristics.

References

Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: a quality of life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*, **85**, 365-76.

Austin PC, Schull MJ (2003). Quantile regression: a statistical tool for out-of-hospital research. *Acad Emerg Med*, **10**, 789-97.

Austin PC, Tu JV, Daly PA, Alter DA (2005). The use of quantile regression in health care research: a case study examining gender differences in the timeliness of thrombolytic therapy. *Statist Med*, **24**, 791-816.

Avis NE, Crawford S, Manuel J (2005). Quality of life among younger women with breast cancer. *J Clin Oncol*, **23**, 3322-30.

Birkes D, Dodge Y (1993). Alternative Methods of Regression. Wiley, Inc.: New York, NY.

Brenner H, Ziegler H, Stegmaier C (2005). Persistence of restrictions in quality of life from the first to third year after diagnosis in women with breast cancer. *J Clin Oncol*, **23**, 4945-53.

Buchinsky M (1994). Changes in the U.S. wage structure 1963–1987: application of quantile regression. *Econometrica*, **62**, 405-58.

Gilchrist WG (2000). Statistical Modeling with Quantile Functions. Chapman & Hall/CRC: Boca Raton, FL.

Green PJ, Silverman B.W (1994). Nonparametric Regression and Generalized Linear Models. Chapman & Hall, London.

Greimel E, Thiel I, Peintinger F, Cegnar I, Pongratz E (2002). Prospective assessment of quality of life of female cancer

patients. *Gynecol Oncol*, **85**, 140-7.
Hartl K, Janni W, Kastner R (2003). Impact of medical and demographic factors on long term quality of life and body image of breast cancer patients. *Ann Oncol*, **14**, 1067-71.
Klee M, Thranov I, Machin D (2000). Life after radiotherapy: the psychological and social effects experienced by women treated for advanced stages of cervical cancer. *Gynecol Oncol*, **76**, 5-13.
Koenker R, Bassett G (1987). Regression quantiles. *Econometrica*, **46**, 33-50.
Koenker R, Bilias Y (2001). Quantile regression for duration data: A reappraisal of the Pennsylvania Reemployment Bonus Experiments. *Empirical Economics*, **26**, 199-220.
Koenker R, Hallock K (2001). Quantile regression. *J Economic Perspect*, **51**, 143-56.
Koenker R, Geling O (2001). Reappraising medfly longevity: A quantile regression survival analysis. *J Am Stat Assoc*, **96**, 458-68.
Lehto VS, Ojanen M, Kellokumpu-Lehtinen P (2005). Predictors of quality of life in newly diagnosed melanoma and breast cancer patients. *Ann Oncol*, **16**, 805-16.
Levin J (2001). For whom the reductions count: a quantile regression analysis of class size and peer effects on scholastic achievement. *Empirical Economics*, **26**, 221-46.
Marcotte DE, Wilcox-Gok VJ (2003). Estimating earnings losses due to mental illness: a quantile regression approach. *Ment Health Policy Econ*, **6**, 123-34.
Safaee A, Moghimi Dehkordi B (2007). Validation study of a quality of life (QOL) questionnaire for use in Iran. *Asian Pacific J Cancer Prev*, **8**, 543-6.