Indian Journal of Pharmacy Practice | Association of Pharmaceutical Teachers of India

Measurement of Quality of Lifein Heart Failure-assessment over two Decades

Radhika. N*, Anoop.P, Praveen Kumar NVRT., Sarvana KRT, Madhusudhan S, Mohanta GP, Manna PK

Division of Pharmacy Practice, Department of Pharmacy, Annamalai University, Annamalai Nagar-608002.

ABSTRACT

Submitted: 17/02/2012 *Accepted: 22/03/2012*

The Quality of Life (QoL), representing a patient-aimed end point in treatment, it has been increasingly emphasized in new heart failure therapies and non – pharmacological therapy. The measurement of QoL depends on the use of validated questionnaire, and with attention paid to the timing of collection of data and also follows up 1 & 2 after patient counselling. Its analysis of data may occur mainly in the context of conventional morbidity and mortality end points. In a review of QoL measurement in heart failure published form 1985 to 2005, we found some important data, such as the number of participating subjects in which those patients benefited by the intervention, and some who are not benefited. QoL is analysed as a treatment end point with consideration of the disease with co-morbidity and heart failure disease alone. Improvement in making QoL questionnaire and patient counselling about disease and medications may be helpful to find out the data in the determination of drug efficacy in heart failure.

Keywords: Heart Failure, Quality of Life.

INTRODUCTION

QoL measurement has been useful for the health care team about the drug therapy and its efficacy of treatment[1,2]. The driving force behind this trend is the recognition that traditional end points, centred on biologic and physiologic outcomes, may not reflect the impact of the interventions on patients QoL. In advance, the patients increasingly involved the complications about medical choices and resources allocation, QoL has become an important aspect of the evaluation process, espeicall in chronic morbidity conditions such as heart failure[3-5] that are characterized by progressive worsening the disease symptoms.

QoL has been defined as the "facets' of our lives that are dominated or significantly influenced by our mental or physical well being"[6]. Various questionnaire have been used to measure QoL; and it is a multi – dimensional construct that can be assessed on the basis of four principal components: physical condition, psychological well-being, social activities and everyday activity[2].

In portentously, health status measures are incorporated into either disease-specific or questionnaire. Some elements such as social or sexual functioning are disease independent; that is, they are likely to be important contributors to QoL regardless of the underlying condition; it measures in questionnaire and allow for different follow up comparisons in patient counselling. In the patient counselling, generally questions focus on symptoms that characterize the disease and their impact on the patient's perception of health. In heart failure, a variety of disease-specific questions have been used[7,8] or have recently been developed[9]. In simple fact that a questionnaire has a follow up in a given disease should not lead automatically to the conclusion that the patient counselling can be used to measure QoL during different follow up of the patient.

Independent of disease, state, interpretation of QoL data requires a critical analysis of the questionnaire used, the way in which the questionnaire is data analyzed, and the frequency and timing of collection of questionnaire data. These are also important considerations in the design of a questionnaire.

The Syndrome of Heart Failure

In traditional view that heart failure is a constellation of signs and symptoms caused by inadequate performance of the heart focuses on only one aspect of the pathophysiology involved in the syndrome. Currently, a complex blend of structural, functional and biologic alterations are evoked to account for the progressive nature of heart failure and to explain the efficacy or failure of therapies used in the treatment[10]. For example, the rationale for the use of beta-blockers in a patient with a poorly contracting heart is based on a conceptual framework broader than that which suggests the treatment of congestion with diuretics or digoxin. The rationale for using beta-blockers is predicated on an understanding of the role of the sympathetic nervous system in promoting the release of rennin and other vasoactive susbstances that trigger vasoconstriction, tachycardia, and changes in myocytes that lead to disadvantageous ventricular dilatation.

***Address for Correspondence:**

Radhika. N, Division of Pharmacy Practice, Department of Pharmacy, Annamalai University, Annamalai Nagar-608002.

Criteria for QoL questionnaire

Three criteria need to be considered in questionnaire development and selection: reliability, validity and responsiveness. The degree to which any given questionnaire meets these criteria should be the major consideration in the decision and the data to use for the quality of life. In reliability is a measure of the degree to which an questionnaire on results repeated follow up at closely related time points under the same conditions. If there is significant variation from follow-up to follow-up, the questionnaire cannot be termed reliable. Validity refers to whether an questionnaire is measuring what it is supposed to measure and is also "demonstrated by showing that changes in the instrument being investigated correlate with changes in other related measures in the theoretically derived predicted direction and magnitude"[3]. The former, external validity, essentially requires that QoL correlates with some other predetermined gold standard outcome, which is often difficult to define and to collect. The latter, internal or construct validity, address psycho metric aspects of the questionnaire and the relatedness of similar measures within the questionnaire.

Responsiveness is a measure of the association between the change in the observed score and the change in the true value of the construct. If a questionnaire is responsive, it will detect even small changes, in both magnitude and direction, in patients who have improved or deteriorated compared with patients who have not changed and for whom the score should remain more or less the same. The QoL is not a static concept, but rather is subject to change as a result of an intervention and or progression of the underlying disease process.

Consideration in QoL questionnaire development

Reliability

- Validity
- Responsiveness
- Relative weighting of domains
- Timing of collecting data about questionnaire
- Frequency of collecting data in disease condition

Timing of QoL collecting data of questionnaire

The data derived from QoL collecting data may be very dependent on the timing of administration, nevertheless, it may be difficult to anticipate the rate of change (either improvement or deterioration) in QoL. The magnitude and timing of these changes may depend on the chronicity and severity of the heart failure, type of intervention, and individual domain under study. For example, a drug could improve social functioning soon after drug administration but have lag effect on other domains. This would have a variable impact on the QoL score, depending on the degree to which social functioning contributes to the questionnaire.

Missing data

Multiple follow-up of a QoL questionnaire can lead to other biases. For example, subjects who are well may be more likely to complete a QoL questionnaire than those who are not well. missing data can significantly impact the way in which data are analyzed. Among other statistical techniques, patients who die can be assigned the "worst possible" score on the questionnaire. Nevertheless, QoL may have been excellent up until the time of death, if the demise was sudden. This problem also exists for non responders who are alive. For this group, attempts can be made, however difficult, to impute a score based on finding correlations between prior responses.

QoL measurement in Heart failure from 1985 to 2005

With this theoretical background and in light of the fact that QoL has been frequently measured in intervention of drug therapy in heart failure, we reviewed the performance of QoL questionnaire in these studies with an emphasis on the appropriateness of the instruments used, the quality of the data obtained, and the way in which the results have been presented.

We performed an extensive MEDLINE and PUBMED search of peer-reviewed publications covering the years of 1985 to 2005 inclusive for citations of QoL, health status, or questionnaires referenced with heart failure, drug therapy, angiotensin-converting enzyme inhibitor, anigotensin receptor blocker, vasodilator, beta adrenergic receptor blocker, digoxin, cardiac glycoside, diuretic, calcium channel blocker, inotrope, alpha adrenergic blocker. We excluded studies that measured QoL in the context of coronary artery bypass graft or valvular surgery, exercise rehabilitation or training, ventricular assist devices, pacemakers, implantable cardioverter, defibrillators. We performed a second MEDLINE and PUBMED search using the names of the questionnaire for the QoL included in this analysis and referenced them to heart, heart failure, and cardiac disease.

A total of 62 studies were identified but only 45 included an actual measurement of QoL. Of this group, 28 met study criteria (regular follow-up and intervention); and 17 were multicenter; and publication dates ranged from 1985 to 2005 [11-35]. The number of patients participating in the studies ranged from 20 to 5339 (median, 131); most studies (n=28) enrolled fewer than 650 patients. Most of the studies enrolled subjects with mild-to-moderate (NYHA class II and III) failure (n=40). Study medications included angiotensin-converting enzyme inhibitors (n=14), beta adrenergic receptor blockers (n=5), vasodilators (n=3), calcium channel blockers (n=5), digoxin (n=6) and others (n=8) and 6 studies

included drugs of more than one class. Duration of patient follow-up ranged from 2 to 144 weeks) (3 to 14 weeks in 16; 15 to 28 weeks in 12; 28 to 56 weeks in 9; and greater than 62 weeks in 4).

All cause mortality was a primary or secondary end point in 12 studies; an additional 23 studies included mortality data but type of end point was not specified. Five of these studied showed statistically significant improvement in survival with the study drug, whereas 6 showed increased mortality with the study drug. Other frequently measured end points were hospitalization and exercise distance.

QoL Measurements

18 generic and 17 disease-specific questionnaire were used with the sickness impact profile (6 studies) and the Minnesota Living With Heart Failure Questionnaire (12 studies) administered most frequently in the 3 categories, respectively. Three generic questionnaire (Nottingham Health Profile, Sickness Impact Profile, and the General Well - Being Index) have been used in cardiac disease states [34,35]. However, data are limited in heart failure [36-38], and we identified no validation studies using these instruments in this population. Conversely, validation data exist for 4 of the disease –specific questionnaire (Minnesota Living With Heart Failure Questionnaire, Chronci Heart Failure Questionnaire, Quality of Life Questionnaire in Severe Heart Failure, and Kansas City Cardiomyopathy Questionnaire)[3,8, 15,16, 39,40, 41].

Quality of Life Questionnaires used in the Study of Heart Failure

Specific	Generic
Minnesota Living With Heart Failure Questionnarie[14]	Sickness Impact Profile[5]
Chronic Heart Failure Questionnaire[2]	General Well-Being Index [3]
Quality of Life Questionnaire in Severe Heart Failure[3]	Nottingham Health Profile [2]
Heart Condition Assessment[1]	Sleep Dysfunction Scale[2]
Disease - Specific questionnaire, otherwise not specified [2]	Profile of Mood States[2]
Disease-Specific self - rating scale, otherwise not specified[1]	Daily Dyspnea, fatigue, Quality of life Scores [1]
	Breathlessness, visual Analog Scale, Tirendess, Arthritis Impact Measurement Scale, Health Status Index [1]

Presentation of QoL Data

29 of the 35 studies reported data on 4 separate time points for measurement of QoL, although 4 did not specify when the second measurement was made. 18 studies reported 3 measurements and 17 reported 4 or more measurements. The number of studies specifying the number of subjects to whom the QoL instrument was administered was 25 for baseline measurement (usually at intervention). A smaller percentage of studies specified the number of patients participating in the subsequent follow-up of a patient (17 of 35 for the 2nd, 8 of 16 for the 3rd, and 4 of 8 for the 4th follow-up); likewise, the percentage of randomized subjects completing questionnaire in these studies decreased (68%, 72%, 58% and 45% for baseline, 2nd, 3rd, and 4th questionnaire respectively). No accounting of the tendency for sicker patients to refrain from participating in QoL questionnaire was made in any study.

A significant improvement in either total or individual domain score was observed in the active treatment arm in 18 studies at 2nd, 3rd and 4th questionnaire. Overall, by type of drug, of 8 angiotensin-converting enzyme inhibitor, 2 of 3 calcium channel blocker, 2 of 5 vasodilator, 1 of 3 digoxin, 2 of 6 beta adrenergic receptor blocker, studies showed improvement in some parameter of QoL.

In one fourth of the studies with at least 3 QoL questionnaire, the investigators did not specify whether the comparisons were made between control and test of active arms after randomization or with their respective baseline scores obtained at the time of randomization or intervention. Statistical analysis was not performed or reported in 5 of 35 studies with 4 questionnaire and 6 of 18 studies with 4 questionnaires measurements.

Timing of QoL Administration

In performed studies detailing the timing of QoL administration, the 2nd, 3rd and 4th measurements were made at 16.7± 24.3, 18.3 ±15.5, and 35.7 ±36.1 weeks from the initial baseline measurement.

To assess whether the timing of administration is commensurate with the underlying trajectory of the disease, we analyzed whether the timing of separation of actuarial curves for other primary or secondary end points was detailed. Such data were presented in only 9 of 35 studies.

Correlations

Among the 19 studies reporting improvement in some parameter of QoL, 9 were accompanied by an improvement in exercise tolerance (eg. Peak oxygen consumption and exercise distance); conversely, 8 studies showed improvement in exercise indices but had no change in QoL. Only 8 studies showed descriptive or statistical correlations between changes in QoL scores and clinical end points, and the relationship between the timing of the change in QoL scores with the timing of change in other end points was not described in any reference in studies.

CONCLUSION

In our review of QoL data from published heart failure studies from 1985 to 2005. We found that the number of subjects participating was often not specified; frequently, no accounting was made for patients who did not participate in serial measurements and no effort was made to determine if the timing of administration of QoL questionnaire makes sense in terms of the clinical trajectory of the disease. We found no studies in which the timing of questionnaire of QoL was compared with the timing of changes in other end points.

Questionnaire that have not been validated in the heart failure population were used. Even among validated questionnaires, criticism exists, including lack of responsiveness to clinical change and the limited range of clinical domains that are quantified. [9]. The implications for drug therapy and intervention was made, and approval and patient well being loom large. Given these findings, we suggest that improvements in methodology are required if quality –of-life data are to add useful insight into the impact of drug therapy on patient morbidity. The implications for drug development and approval and patient well-being loom large.

REFERENCES

1. Tsevat J, Weeks JC, Guadagnoli E, Tosteson AN, Mangione CM, Pliskin JS, Weinstein MC, Cleary PD. Using health-related quality of life information: clinical encounters, clinical trials, and health policy. J Gen Intern Med 1994;9:576-82.
2. Luderitz B, Jung W, Quality of life in patients with atrial fibrillation. Arch Intern Med 2000;160: 1749-57.
3. Guyatt GH; Measurement of health – related quality of life in heart failure. J Am Coll Cardiol 1993;22[supplA]: 185A-91A.
4. Doba N, Tomiyama H, Nakayama T. Drugs, heart failure and quality of life. Drugs Aging 1999;14:153-63.
5. Dracup K, Walden JA< Stevenson LW, Brecht ML: Quality of life in patients with advanced heart failure. J Heart Lung Transplant 1992;11:273-9.
6. Ware Je Jr, Snow KK, Knsinki M, Gandek B: SF-36, Health survey manual and interpretation guide. Nimrod, Boston, pp993.
7. Guyatt GH, Nogradi S, Halcrow S, Singer J, Sullivan MJJ, Fallen EL: Development and testing of a new measure of health status for clinical trial sin heart failure. J Gen Intern Med 1989;4:101-7.
8. De Vries RJM, Quere M, Lok DJA, Sijbring P, Bucx JJ, van Veldhusien DJ, Dunselman PH. Comparison of effects on peak oxygen consumption, quality of life, and neurohormones of felodipine and enalapril in patients with congestive heart failure. Am J Cardiol 1995;76:1253-8.
9. Green CP, Porter CB, Bresnahan Dr, Spertus JA; Development and evaluation of the Kansas City Cardiomypoathy Questionnaire: A new health status measure for heart failure. J Am Coll CArdiol 2000; 35:1245-55.
10. Mariell Jes sup, Susan Brozena, Heart Failure, N Engl J Med 2003;348:2007-18.
11. Waagstein F, Bristow MR, Swedberg K, Camerini F, Fowler MB, Silver MA, for the metoprolol in dilated Cardiomyophathy (MDC) trial sudy group: Beneficial effects of metoprolol in idiopathic dilated cardiomyopathy. Lancet 1993; 342:1441-6.
12. Packer M, Colucci WS, Sackner-Bernsein JD, Liang Cs, Goldscher DA, Freeman I, for the PRECISE study group: Double blind, placebo – controlled study of the effects of carveiol in patients with moderate to severe heart failure. Circulation 1996;94:2793-9.
13. Colucci WS, Packer M, Bristow MR, Gilbert EM, Cohn JN, Fowler MB, for the US Carvediol Heart Failure Study Grooup: Carvediol inhibits clinical progression in patients with mild symptoms of heart failure. Circulation 1997;94:2800-6.
14. Briwtow MR, Gilbert EM, Abraham WT, Adams KF, Fowler MB, Hershberger RE, for the MOCH Investigators: Carvedilol produces dose-related improvements in left Ventricular Function and survival in subjects with chronic heart failure. Circulation 1996;94:2807-16.
15. Konstam V, Salem D, Pouteur H, Kosus J, Gorkin L, Shumaker S, Mottard I, Woods P, Konstam MA, Yusuf S. Baseline quality of life as a predictor of mortatlity and hospitalization in 5025 patients with congestive heart failure. Am J Cardiol 1996;78:890-5.
16. Rogers WJ, Johnstone De, Yusuf S, Weiner DH, Gallaher P, Bittner VA, Ahn S, Schron E, Shumaker SA, Sheffield LT, Quality of life among 5,025 patietns with left ventricular dysfunction randomized between placebo and enalapril: the studies of left ventricular dysfunction. J Am Coll Cardiol 1994;23:393:400.
17. Rector Ts, Kubo SH, Cohn JN: Validity of the Minnesota Living with heart Failure Questionnaire as a measure of therapeutic response to enalapril or placebo. Am J Cardiol 1993;71:1106-7.
18. Cohn JN, Johnson G, Ziesche S, Cobb F, Francis G, Tristani F, Smith R, Dunkman WB, Loeb H, Wong M. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatient of chronic congestive heart failure. N Engl J Med 1991;325:303-10.
19. Reactor TS, Johnson G, Dunkman B, Daniels G, Farrell L, Hendrick A, for the V-HeFT VA Cooperative studies Group: Evaluation by patients with heart failure of the effects of enalapril compared with hydralazine plus isosorbide dinitrate

on quality of life. Circulation 1993; 87 [suppl VI]:VI-71-VI-77.

20. Bulpitt CJ, Fletcher AE, Dossegger L, Neiss A, Nielsen T, Viergutz S, for the cilazpril-captopril Multicentre Group: Quality of life in chronic heart failure: Cilazapril and captopril versus placebo. Heart 1998;79:593-8.
21. Northride DB, Rose E, Raftery Ed, Lahiri A, Elder At, Shaw TR, Henderson E, Dargie HJ. A multicentre, double-blind, placebo-controlled trial of quinapril in mild, chronic heart failure. Eur Soc Cardiol 1993;14:403-9.
22. Mckelvie Rs, Yusuf S, Pericak D, Avezum A, Burns RJ, Probstfield J, Tsuyuki RT, White M, Rouleau J, Latini R, Maggioni A, Young J, Pogue J. Comparison of candesartan, enalapril, and the combination in congestive heart failure. Randomized evaluation of strategies for left ventricular dysfunction pilot study. The pilot study investigators. Circulation 1999;100:1056-64.
23. Cohn JN, Ziesche S, Smith R, Anand I, Dunkman WB, Loeb H, for the Vasodilator Heart Failure Trial study group: Effect of the calcium antagonist felodipine as supplementary vasodilator therapy in patients with chronic heart failure treated with enalapril. Cicuraltion 1997;96:856-63.
24. Guyatt GH, Sullivan MJJ, Fallen EL, Tihal H, Rideout E, Halcrow S, Nogradi S, Townsend M, Taylor Dw. A controlled trial of digoxin in congestive heart failure. Am J Cardiol 1988;61:371-5.
25. Hampton JR, van Veldhuisen DJ, Kleber FX, Cowley AJ, Ardia A, Block P, for the second prospective randomized study of Ibopamine on mortality and efficacy investigators: Randomized study of effects of ibopamine on survival in patients with advanced severe heart failure. Lancet 1997;349:971-7.
26. Kubo SH, Gollub S, Bourge R, Rahko P, Cobb F, Jessup M, for the pimobendan multicenter research group: beneficial effects of pimobendan on exercise tolerance and quality of life in patients with heart failure. Cirucation 1992;85:942-9.
27. The pimobendan in congestive hart failure investigators. Effect of pimobendan on exercise capciaty inpatients with heart failure: main results from the pimobendan incongestive heart failure trial., heart 1996:76:223-31.
28. Cowley AJ, Skene AM, the Enoximone Invetigators: Treatment of severe heart failure: quantity or quality of life? A trial of enoximone. Br Heart J 1994:72:226-30.
29. Waller Dg, Webster J, Sykes CA, Bhalla KK, Wray R: Clincial efficacy of xamoterol, a beta one adrenoceptor partial agonist, in mild to moderate heart failure. Eur Soc Cardiol 1989;10:1003-10.
30. Kubo SH, Rector TS, Strobeck JE, Cohn JN:OPC – 8212 in the treatment of congestive heart failure: results of a pilot study. Cardiovascular Drug Ther 1988;2:653-60.
31. Elkayam U, Johnson JV, Shotan A, Bokhari S, Solodky A, Canetti M, Wani OR< Karaalp Is. Double-blind, placebo controlled study to evaluate the effect of organic nitrates inpatients with chronic heart failure treated with angiotensin-converting enzyme inhibition. Circulation 1999;99:2652-7.
32. Doreszewski A, Gohmann E, Dorszewski B, Werner Gs, Kreuzer H, Figulla HR: Vasodilation by urapidil in the treatment of chronic congestive heart failure in addition to angiotensin conveting enzyme inhibitors is not beneficial:results of a placebo-controlled, double-blind study. J Card Fail 1997;3:91-6.
33. Deswar A, Bozkurt B, Seta Y, Parilit-Eiswirth S, Hayes Fa, Blosch C, Mann DL. Safey and efficacy of a soluble P75 tumor necrosis factor receptor (Enbrel, Etanercept) in patients with advanced hart failure. Circulartio 1999;99:3224-6.
34. Lau CP, Rushby J, Leigh-Jones M, Tam CY, Poloniecki J, Ingram A, Sutton R, Camm AJ, Symptomatology and quality of life in patients with rate responsive pacemakers: a double blind, randomized, crossover study. Clin Cardiol 1989;12:505-12.
35. Marwick TH, Zuchowski C, Lauer MS, Secknus M-A, Williams J, Lytle BW: Functional status and quality of life in patients with heart failure undergoing coronary bypass surgery after assessment of myocardial viability. J Am Coll Cardiol 1999;33:750-8.
36. Ekeberg O, Klemsdal TO, Kjeldsen Se: Quality of life on enalpril after acute myocardial infarction. Eur Heart J 1994;15:1135-9.
37. Goodyer LI, Miskelly F, Millgan P: Does encouraging good compliance improve patietns' clinical condition in heart failure? Br J Clin Pract 1995;49:173-6.
38. Cline CMJ, Willenheimer RB, Erhardt LR, Wilund I, Israelsson BYA: Health –related quality of life in elderly patients with heart failure. Scand Cardiovasc J 1998;33: 278-85.
39. Wiklund I, Lindvall K, Swedberg K, Zupkis RV: Self-assessment of quality of life in severe heart failure. Scand J Psychol 1987;28:220-5.
40. Rector Ts, Kubo SH, Cohn JN: Patients' self assessment of their congestive heart failure: II. Content, reliability and validity of new measure-the Minnesota Living With Heart Failure Questionnaire. Heart Fail 1987;3:198-209.

Guyatt GH, Sullivan MJJ, Fallen EL, Tihal H, Rideout E, Halcrow S,Nogradi S, Townsend M, Taylor DW. A controlled trial of digoxin in congestive heart failure. Am J Cardiol 1988;61:371-5