

Comparing quality of life following liver transplantation for Laennec's versus non-Laennec's patients¹

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Abstract: The overall success of orthotopic liver transplantation (OLT_X) includes not only survival, but quality of life (QOL) as well. We studied one controversial group of OLT_X recipients, patients transplanted for alcoholic liver disease (Laennec's), to determine if their post-OLT_X QOL was similar to that of patients transplanted for non-alcoholic liver disease (non-Laennec's). Over a 10-yr period, patients undergoing OLT_X at our institution were asked to complete a QOL questionnaire addressing a wide range of topics from demographics and employment to symptom distress/frequency, activities of daily living, and effect of loss of health on daily life. Twenty-four Laennec's and 100 non-Laennec's OLT_X recipients completed the questionnaire at both their 2- and 5-yr follow-up visits at our institution. Both groups were well-matched in age, race, and patient location status at the time of OLT_X. No significant differences could be detected between Laennec's and non-Laennec's scores regarding overall QOL, including one's ability to function, health perception, and self-perception at 2 and 5 years post-OLT_X, and between 2 and 5 years post-OLT_X. Although not between groups, a significant difference was noted regarding patients' satisfaction with life, with less satisfaction reported at the 5-yr versus the 2-yr time point post-OLT_X. Rates of current/recent employment between both groups were also similar at 2 years post-OLT_X, and again at 5 years post-OLT_X. We conclude that overall QOL and employment levels appear similar between patients transplanted for alcoholic and non-alcoholic liver disease. This similarity appears to extend to 5 years post-OLT_X.

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Orthotopic liver transplantation (OLT_X) has become the treatment of choice for end-stage liver disease of various etiologies. Focus on its application has expanded to include not only patient survival, but monetary cost and social impact as well (1). With the expense of OLT_X averaging around \$288 000 per patient within the 1st year (2), issues such as quality of life (QOL) and long-term functional recovery have become an important

means of evaluating cost-utility and cost-effectiveness of this therapy.

Most past studies examining QOL among liver transplant patients have reported on improvements made within the transplant population as a whole, generally irrespective of variance in patients' pre-OLT_X diagnoses (3–7). Some investigators, however, have reported conflicting findings on patients' QOL in light of patients' pre-OLT_X illnesses, in particular, alcoholic versus non-alcoholic liver disease (8, 9). With alcoholic liver disease having taken center-stage as one of the leading causes for adult liver transplantation within the United States

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(10), the need for more conclusive study on this topic has become evident. The aim of this study was to compare the QOL of OLTX recipients transplanted for alcoholic liver disease, Laennec's cirrhosis, with that of OLTX recipients transplanted for non-alcoholic liver disease for a period extending to 5 years post-OLTX.

Patients and methods

From October 1989 to July 1994, 628 adult patients underwent OLTX at our institution. All patients transplanted during that period were asked to complete a QOL questionnaire at their initial pre-OLTX evaluation and again post-OLTX at 1-, 2- and 5-yr follow-up visits at our institution. Administration of the assessment tool was self-report with no restrictions placed on patients' obtaining help from others to complete the form. This questionnaire, a modified version of the National Institute of Diabetes, Digestive and Kidney Diseases liver transplantation QOL form (4), addressed a wide range of topics describing patient demographics, employment, symptom distress and frequency, activities of daily living, and effect of loss of health on daily life. Core questions came from well-recognized and validated instruments measuring QOL among the acutely and the chronically ill, including: the Karnofsky Performance Status Scale, the Sickness Impact Profile, the Index of Well-Being, the Medical Outcomes Survey (MOS 20), and the Nottingham Health Profile (3, 11–16). All of these indices in their original form were designed to be interviewer-administered, whereas our questionnaire was designed for self (patient)-administration. Because all the instruments compiling our QOL questionnaire were considered valid measuring tools, our instrument, in turn, was also considered a valid measuring tool. Internal consistency reliability of our questionnaire was tested, resulting in a Cronbach's coefficient alpha of 0.97.

Patients completing our QOL questionnaire at both their 2- and 5-yr follow-up visits at our institution were categorized into one of two groups based on their pre-OLTX diagnoses; Laennec's and non-Laennec's. Criteria used for diagnosing alcoholic liver disease included a patient's history of alcohol abuse/dependence as determined by psychiatric and/or psychosocial evaluation and compatible histology on biopsy and hepatectomy specimens. Patient selection criteria for OLTX included the absence of medical contraindications, favorable psychosocial and/or psychiatric assessment, demonstrated pre-OLTX sobriety, and compliance with medical management. A patient's

location (home, hospital, ICU) just prior to transplant was used in place of the United Network for Organ Sharing (UNOS) status scale for clarification purposes, as the numbers used to represent one's UNOS status have been associated with various meanings within the past few years.

For scoring purposes, 88 of the 122 items on the questionnaire were grouped into one of three categories and scored only once (the remaining 34 items were descriptive and not designed for scoring). The three categories broadly highlighted one's ability to function, health perception, and self-perception as described below:

Ability to function. This group of questions assessed patients' ability to be active within their home, social, and work lives. Its subcategory focused on health limits in activities by assessing any remaining and/or newly acquired limitations following OLTX.

Self-perception. This category examined a patient's self-image post-OLTX and included sub-scores for symptom frequency (highlighting changes in patients' bodily appearance, function, and/or emotional state), symptom distress (affliction resulting from physical and/or emotional changes), and patients' feelings about life (differentially assessing patients' satisfaction with life using adjectives such as: enjoyable vs. miserable, easy vs. hard, disappointing vs. rewarding, etc.).

Health perception. This category examined a patient's perception of his or her health and included a subcategory assessing the frequency of additional physical symptoms not assessed within the 'self-perception' category.

All category and subcategory scores were scaled equally from 0 to 100 points to allow for suitable comparisons. Higher scores, in all instances, reflected better QOL. Inclusion of all 88 scoreable questions constituted one's overall QOL score. Post-OLTX employment data at both 2 and 5 years post-OLTX were also compared, although the structure of these questions was not amenable to a scoring system. Pre-OLTX and 1-yr post-OLTX data, although available, were deliberately not analyzed for this study as previous findings from our institution have shown that OLTX continues to improve beyond the 1st year post-OLTX (4). For the present investigation, we elected to study those patients in whom QOL may have stabilized.

Comparisons between scores at different time points were made using one-way analysis of variance (ANOVA). Follow-up comparisons between time points were performed using 2-factor repeated measures ANOVA. Categorical data were com-

Table 1. Primary diagnosis of liver disease for Laennec's and non-Laennec's patients

	Laennec's (n = 24)	Non-Laennec's (n = 100)
Autoimmune	0	6
Cryptogenic cirrhosis	0	18
Sub/fulminant hepatic failure	0	5
Hepatocellular carcinoma	0	2
Hepatitis B	0	6
Hepatitis C, non A, non B	2	19
Laennec's	21	0
Metabolic	1	2
Other	0	6
Other malignancy	0	2
Primary biliary cirrhosis	0	20
Primary sclerosing cholangitis	0	14

Table 2. Patient demographics at time of OLT_X

Variable	Laennec's (n = 24)	Non-Laennec's (n = 100)
Age (yr)*	p = 0.823	
0-50	54% (13)	51% (51)
>50	46% (11)	49% (49)
Race	p = 1.000	
White	92% (22)	90% (90)
Non-white	8% (2)	10% (10)
Sex	p < 0.0001	
Male	92% (22)	43% (43)
Female	8% (2)	57% (57)
Pt. location status	p = 0.325	
Home	71% (17)	76% (76)
Hospital	25% (6)	14% (14)
ICU	4% (1)	10% (10)

* Mean age of Laennec's = 51 ± 8; non-Laennec's = 50 ± 12 (SD)

pared using Fisher's exact test for 2 × 2 tables and likelihood ratio χ^2 for higher-dimension tables. A p-value < 0.05 was considered significant.

Table 3. Patient demographics at 2 and 5 years post-OLT_X

Variable	At 2-yr follow-up		At 5-yr follow-up	
	Laennec's (n = 24)	Non-Laennec's (n = 100)	Laennec's (n = 24)	Non-Laennec's (n = 100)
Education (yr)	p = 0.424		p = 0.225	
≤ 12	42% (10)	28% (28)	42% (10)	32% (32)
≥ 13, < 16	29% (7)	39% (39)	21% (5)	39% (39)
≥ 16	29% (7)	33% (33)	37% (9)	29% (29)
Marital status	p = 0.406		p = 1.00	
Married	75% (18)	82% (82)	79% (19)	81% (80)
Other	25% (6)	18% (18)	21% (5)	19% (19)
Living arrangements	p = 1.00		p = 1.00	
Alone	8% (2)	11% (11)	8% (2)	10% (10)
With family/other	92% (22)	89% (89)	92% (22)	90% (88)

Results

Twenty-four recipients in the Laennec's group and 100 recipients in the non-Laennec's group completed the QOL questionnaire at both their 2- and 5-yr follow-up visits at our institution. Laennec's cirrhosis was found to be the primary diagnosis for nearly all those in the Laennec's group, while primary biliary cirrhosis led as the primary cause of liver disease among those in the non-Laennec's group (Table 1). Patients in both groups appeared to be well-matched regarding age, race, and patient location status at the time of surgery (Table 2). Significant differences were observed, however, between groups regarding sex, with a greater proportion of males comprising the Laennec's group than the non-Laennec's group (Table 2). Along with age, race, and patient location status, the two groups were well-matched in education, marital status, and type of living arrangements at both 2- and 5-yr time points post-OLT_X (Table 3).

No significant differences could be detected between Laennec's and non-Laennec's scores regarding overall QOL at 2 and 5 years, and between 2 and 5 years post-OLT_X. Similarities were also found between scores on overall health perception (including symptom frequency), ability to function (including health limitations), and self-perception (including symptom distress and symptom frequency) at, and between the 2- and 5-yr time points post-OLT_X (Table 4). A significant difference was noted, however, when examining the 3rd subcategory of self-perception, 'feelings about life'. This difference, concerning patients' satisfaction with life, pointed to variance in scores between time periods (2- vs. 5-yr), rather than between groups.

Functional status was assessed by the Karnofsky Performance Status Scale. This scale was originally designed to rank patients' physical functioning per-

Table 4. Overall, category and subcategory QOL scores at 2 and 5 years post-OLT_X (mean \pm SD)

Variable	At 2-yr follow-up		At 5-yr follow-up		p*	p*	p*
	Laennec's	Non-Laennec's	Laennec's	Non-Laennec's	(Group)	(Time)	(Time/group)
Quality of life (overall)	69 \pm 16	74 \pm 16	70 \pm 18	72 \pm 16	0.472	0.297	0.760
Ability to function	68 \pm 20	75 \pm 22	69 \pm 25	73 \pm 22	0.282	0.332	0.607
Health limits	63 \pm 29	77 \pm 27	68 \pm 30	75 \pm 27	0.095	0.864	0.258
Health perception	64 \pm 16	68 \pm 16	64 \pm 19	66 \pm 16	0.396	0.175	0.916
Symptoms	67 \pm 14	71 \pm 15	68 \pm 16	68 \pm 17	0.745	0.297	0.636
Self-perception	71 \pm 16	76 \pm 15	73 \pm 16	75 \pm 15	0.391	0.346	0.847
Symptom distress	72 \pm 19	75 \pm 17	72 \pm 17	73 \pm 18	0.755	0.472	0.490
Symptom frequency	73 \pm 19	70 \pm 22	78 \pm 19	72 \pm 19	0.362	0.160	0.544
Feelings about life	76 \pm 20	80 \pm 18	69 \pm 24	79 \pm 19	0.077	0.007	0.216

* 2-factor repeated measures ANOVA.

formance into one of ten categories based on a health care professional's observations. However, since our questionnaire was self-administered, performance ratings in this instance reflected only the patients' subjective assessments. No significant differences were noted between Laennec's and non-Laennec's at the 2- and 5-yr time points post-OLT_X (Table 5). The majority of patients in both groups at both follow-up periods had rated their physical functionality to be 'normal', having either no signs or symptoms of disease, or having only minor signs or symptoms of disease.

When examining employment status at the time of the survey, no significant differences could be detected between the proportion of Laennec's and non-Laennec's patients having had reported current/recent employment (within the past 12 months) at both 2- and 5-yr time periods post-OLT_X (Table 6). Furthermore, the majority of workers in both groups had reported satisfaction with their jobs at both 2- and 5-yr time points post-OLT_X. Ill-health was the primary reason for non-employment among patients in both groups at both time periods post-OLT_X. Although no sig-

nificant differences could be noted between the groups regarding 'reasons for non-employment', the 2-yr follow-up assessment revealed a greater tendency by those in the Laennec's group than the non-Laennec's group to have credited their absence of employment to ill-health (Table 6).

Although review of patients' alcohol histories revealed only broad categorizations, an effort was made to assess and document in detail any post-OLT_X alcohol use among the Laennec's group. Based upon personal interviews with either the patients and/or their follow-up physicians, the majority, 63%, had reportedly maintained abstinence from the time of their transplant until their 5-yr anniversary. Twenty-five percent were reported to have resumed drinking at an occasional level (four or less drinks per month), 4% at a social level (1–3 drinks per wk), and 8% at an excessive level (eight or more drinks per wk).

Discussion

The purpose of our investigation was to assess potential differences in QOL post-OLT_X between

Table 5. Physical functioning performance at 2 and 5 years post-OLT_X

Karnofsky Performance Status Scale (abbreviated)	At 2 years		At 5 years	
	Laennec's (n = 24)	Non-Laennec's (n = 100)	Laennec's (n = 24)	Non-Laennec's (n = 100)
	p = 0.133		p = 1.00	
1. Normal; no complaints, no evidence of disease				
2. Normal activity; minor signs or symptoms of disease	70% (16)	84% (81)	61% (14)	62% (59)
3. Normal activity with effort; some signs or symptoms of disease				
4. Care for myself but unable to do normal activity or do active work	30% (7)	16% (15)	39% (9)	38% (36)
5. Requiring occasional assistance, care for most of my own needs				
6. Requiring considerable assistance and frequent medical care	0	0	0	0
7. Disabled; requiring special care and assistance				
8. Severely disabled; hospitalization indicated, death not imminent	0	0	0	0
9. Hospitalization needed, very sick, needs active support/treatment				
10. Moribund, fatal processes progressing rapidly	0	0	0	0

patients transplanted for alcohol-related and non-alcohol-related liver disease. Examining data from those who completed the QOL questionnaires at both their 2- and 5-yr follow-up visits allowed for changes to be detected within the same subject from one time period to the other. No efforts were made to exclude from this study any OLT_X recipient on the basis of type of liver disease pre-OLT_X, or recurrence of alcohol use post-OLT_X.

Our findings demonstrated that the overall QOL between Laennec's and non-Laennec's patients appeared similar at, and between, 2 and 5 years post-OLT_X. This similarity extended to include all category and subcategory scores except 'feelings about life'. This difference suggested that OLT_X recipients, both alcohol-related and non-alcohol-related, appeared less satisfied with their lives at 5 years post-OLT_X than at 2 years post-OLT_X. Furthermore, although no significant differences could be observed between the two groups, the decrease in this subcategory's scores from the 2nd- to the 5th-yr interval tended to be more notable among the Laennec's group than the non-Laennec's group. Although physical performance functioning, employment, and job satisfaction rates appeared similar between Laennec's and non-Laennec's at both time periods post-OLT_X, a greater proportion of Laennec's than non-Laennec's tended to associate their non-employment with ill-health at the 2-yr interval post-OLT_X.

Although the data from our investigation clearly depicted a similar QOL between Laennec's and non-Laennec's patients, several limitations of this study should be addressed. First, we used data from only those individuals who completed the questionnaire at both their 2- and 5-yr follow-up visits. While this allowed us to examine changes over time within the same patient, it instituted a selection bias against those who would not, or could not participate. Second, patients were left on

their own to voluntarily complete the forms; thus, patients' answers may have been somewhat skewed since the participants were not prevented from making their form completion a joint effort, as in recruiting the help of a spouse, family member, or friend. Third, patients in the Laennec's and non-Laennec's groups appeared to be well-matched demographically in all examined domains excluding sex. In this arena, the proportion of females in the non-Laennec's group far outweighed the proportion of females in the Laennec's group ($n = 57$ vs. $n = 2$). For this reason we attempted to control for the potential influence of sex on QOL scores by eliminating the females from both groups and re-examining the data using only males (no additional females could be added to the Laennec's group). Once again, a similar overall QOL score was demonstrated between the Laennec's and non-Laennec's groups at, and between, the 2- and 5-yr time points post-OLT_X. Likewise, when examining the individual category and subcategory scores, similarity dominated in all areas except for those assessing ability to function (including limitations), and frequency of symptoms. From this analysis, overall ability to function appeared greater among the non-Laennec's male population than the Laennec's male population. Additionally, both groups reported less ability to function and greater symptom frequency at the 5-yr time point compared with the 2-yr time point post-OLT_X. These findings suggest that although we found no differences between the complete groups (males and females) at both time periods post-OLT_X, disparity in the male-to-female ratio may have played a possible role in masking differences between the two groups regarding health limitations and symptom frequency. Past findings have shown instances wherein females, both healthy and non-healthy, have reported a poorer health-related QOL than that of males (17, 18). Studies involving a larger

Table 6. Employment, job satisfaction, and reasons for non-employment at 2 and 5 years post-OLT_X

Variable	At 2 yr		At 5 yr	
	Laennec's	Non-Laennec's	Laennec's	Non-Laennec's
Employment (current/past yr)				
Not working for pay	53% (10)	38% (34)	60% (12)	42% (35)
Working full/part time	47% (9)	62% (55)	40% (8)	58% (48)
full time only	7/9 (78%)	42/55 (76%)	5/8 (63%)	37/48 (77%)
Job satisfaction				
Satisfied	83% (5)	89% (32)	67% (4)	79% (26)
Dissatisfied	17% (1)	11% (4)	33% (2)	21% (7)
Reasons for non-employment				
Disabled/retired due to ill-health	70% (12)	48% (27)	64.70% (11)	48% (30)
Retired due to age	18% (3)	11% (6)	17.65% (3)	16% (10)
Non-health-related	12% (2)	41% (23)	17.65% (3)	36% (23)

sample size of Laennec's females, allowing adjustment for the influence of sex, should be used to further examine specific issues pertaining to QOL between Laennec's and non-Laennec's populations.

Past studies have demonstrated similar survival rates between alcohol-related and non-alcohol-related OLTX recipients (19–21). Moreover, this similarity has been found to extend to at least 5 years post-OLT (22). In the same manner, QOL, as demonstrated by our study, also appears to be similar between those having undergone OLTX for alcohol-related and non-alcohol-related liver disease. Furthermore, this QOL appears to consist of a stable self-perceived state of emotional and physical health, including a lifestyle of activity, which for many includes an active role within the work force.

In conclusion, this medium- to long-term study depicts that select patients transplanted for alcoholic liver disease are able to maintain a healthy and productive QOL not unlike those transplanted for non-alcohol-related illness. Furthermore, this QOL is sustained to at least 5 years post-OLT. Although liver transplantation is a resource-intensive procedure, the resultant QOL it affords to both alcohol- and non-alcohol-related OLTX recipients appears to provide added justification for its use.

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References

1. LEVY MF, GOLDSTEIN RM, HUSBERG BS et al. Baylor update: outcome analysis in liver transplantation. In: Teraski PI, Cecka JM, eds. *Clinical Transplants*. 1993: 161.
2. KANKAANPAA J. Cost effectiveness of liver transplantation—How to apply the results in resource allocation. *Preventive Med* 1990; 19: 700.
3. BONSEL GJ, ESSINK-BOT ML, KLOMPMAKER IJ, SLOOFF MJH. Assessment of the quality of life before and following liver transplantation. *Transplantation* 1992; 53: 796.
4. LEVY MF, JENNINGS L, ABOULJOD MS et al. Quality of life improvements at one, two, and five years after liver transplantation. *Transplantation* 1995; 59: 515.
5. PRICE CE, LOWE D, COHEN AT et al. Prospective study of the quality of life in patients assessed for liver transplantation: outcome in transplanted and not transplanted groups. *J R Soc Med* 1995; 88: 130.
6. LUNDGREN M, KRISTIANSSON M, ERICZON BG, ELEBORG L. Improved quality of life after liver transplantation. *Transpl Proc* 1994; 26: 1779.
7. BELLE SH, PORAYKO MK, HOOFNAGLE JH, LAKE JR, ZETTERMAN RK. Changes in quality of life after liver transplantation among adults. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Liver Transplantation Database (LTD). *Liver Transpl Surg* 1997; 3: 93.
8. BERESFORD TP, SCHWARTZ J, WILSON D, MERION R, LUCEY M. The short-term psychological health of alcoholic and non-alcoholic liver transplant recipients. *Alcohol Clin Exp Res* 1992; 16: 996.
9. WIESNER RH, LOMBARDERO M, LAKE JR, EVERHART J, DETRE KM. Liver Transplantation for end-stage liver disease: an assessment of outcomes. *Liver Transpl Surg* 1997; 3: 231.
10. BELLE SH, BERINGER KC, DETRE KM. Liver transplantation for alcoholic liver disease in the United States: 1988 to 1995. *Liver Transpl Surg* 1997; 3: 212.
11. TARTER E, SWITALA J, ARIA A, VAN THIEL DH. Impact of liver disease on daily living in transplantation candidates. *J Clin Epidemiol* 1991; 44: 1079.
12. KARNOFSKY DA, BURCHENAL JR. In: Macleod C, ed. *Evaluation of Chemotherapeutic Agents*. New York: Columbia University Press, 1949: 191.
13. CAMPBELL A, CONVERSE PE, RODGERS NL. *The quality of American life*. New York: NYL Russell Sage Foundation, 1976.
14. KATZ S, FORD AB, MOSKOWITZ RW, JACKSON BA, JAFFE MW. The index of ADL: a standardized measure of biological and psychosocial function. *J Am Med Assoc* 1963; 185: 914.
15. GILSON BS, GILSON JS, BERGNER M et al. The sickness impact profile: development of an outcome measure of health care. *Am J Public Health* 1975; 65: 1304.
16. BERGNER M, BOBBITT RA, POLLARD WE, MARTIN DP, GILSON BS. The sickness impact profile: validation of a health status measure. *Med Care* 1976; 14: 57.
17. BONKOVSKY HL, WOOLLEY JM. Consensus Interferon Study Group. Reduction of health-related quality of life in chronic hepatitis C and improvement with interferon therapy. *Hepatology* 1999; 29: 264.
18. WARE JE, SNOW KK, KOSINSKI M, GANDEK B. *SF-36 Health Survey Manual and Interpretation Guide*. Boston, MA: New England Medical Center, The Health Institute, 1993.
19. KUMAR S, STAUBER RE, GAVALER JS et al. Orthotopic liver transplantation for alcoholic liver disease. *Hepatology* 1990; 11: 159.
20. LUCY MR, MERION RM, HENLEY KS et al. Selection for and outcome of liver transplantation in alcoholic liver disease. *Gastroenterology* 1992; 102: 1736.
21. GERHARDT TC, GOLDSTEIN RM, URSCHER HC et al. Alcohol use following liver transplantation for alcoholic cirrhosis. *Transplantation* 1996; 62: 1060.
22. BERLAKOVICH GA, STEININGER R, HERBST F, BARLAN M, MITTLBOCK M, MUHLBACHER F. Efficacy of liver transplantation for alcoholic cirrhosis with respect to recidivism and compliance. *Transplantation* 1994; 58: 560.