



2016 Liver Transplantation: Global view

From prolonging life to prolonging working life: Tackling unemployment among liver-transplant recipients

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Abstract

Return to active and productive life is a key goal of modern liver transplantation (LT). Despite marked improvements in quality of life and functional status, a substantial proportion of LT recipients are unable to resume gainful employment. Unemployment forms a threat to physical and psychosocial health, and impairs LT cost-utility through lost productivity. In

studies published after year 2000, the average post-LT employment rate is 37%, ranging from 22% to 55% by study. Significant heterogeneity exists among studies. Nonetheless, these employment rates are lower than in the general population and kidney-transplant population. Most consistent employment predictors include pre-LT employment status, male gender, functional/health status, and subjective work ability. Work ability is impaired by physical fatigue and depression, but affected also by working conditions and society. Promotion of post-LT employment is hampered by a lack of interventional studies. Prevention of pre-LT disability by effective treatment of (minimal) hepatic encephalopathy, maintaining mobility, and planning work adjustments early in the course of chronic liver disease, as well as timely post-LT physical rehabilitation, continuous encouragement, self-efficacy improvements, and depression management are key elements of successful employment-promoting strategies. Prolonging LT recipients' working life would further strengthen the success of transplantation, and this is likely best achieved through multidisciplinary efforts ideally starting even before LT candidacy.

Key words: Employment; Workforce; Transplantation; Quality of life; Work ability

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Core tip: Outcomes after liver transplantation are steadily improving and transplant recipients are increasingly able to resume normal life. However, a considerable number of recipients are unable to resume work, and this represents an increasing challenge in the field of liver transplantation. This paper discusses possible barriers to post-transplant employment, and means to increase return-to-work among liver transplant recipients.

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INTRODUCTION

Liver transplantation (LT) has been established therapy for various end-stage liver diseases for more than 3 decades. With around 90% of LT recipients currently surviving the first postoperative year^[1,2] and with the subsequent life expectancy now exceeding 20 years^[3,4], functional outcomes and quality-of-life issues are attracting increased attention. The goal of modern LT can no longer be considered merely to prolong survival, but to achieve complete functional recovery and psychosocial re-integration with a return to active and productive life.

Questionnaire-based studies demonstrate comparable quality of life of LT recipients and in the general population with some deficits mainly in physical dimensions^[5,6]. In spite of this, a substantial proportion of LT recipients are unable to resume gainful employment, which can be regarded as an objective and rough indicator of quality of life and functional outcome.

In this context, the relevance of employment depends on the point of view. From the patient's perspective, being employed is associated with better quality of life^[6,7], increased sense of confidence, structure, purpose and meaning^[8], improved psychosocial adaptation, financial stability, and a more balanced equilibrium in the family system^[9]. From the transplant professional's perspective, employment serves as a surrogate marker of patients' functional status, and as such becomes a relevant outcome parameter. From the societal/payer perspective, employment improves LT cost-utility by reducing costs from lost productivity, and thus high post-LT employment rates can support the rationale for transplantation funding.

The most comprehensive review of employment after LT by Bravata *et al*^[10] published in 2001 included 82 studies from the 1980s and 1990s. They reported that, respectively, 33% of patients with underlying alcoholic liver disease (ALD) and 80% with non-ALD had resumed work at 3 years post-LT. Since then, the landscape of LT has evolved, with changing patient characteristics, and quality-of-life and employment issues have assumed increased focus in clinical practice.

This review, with a focus on studies published after year 2000, summarizes current employment rates after LT, factors associated with (un)employment, and potential strategies to support and promote ability to

resume work after LT.

OCCUPATIONAL RESTRICTIONS AFTER LT

Return to work is usually allowed once incisions have healed and the patient is able to perform daily activities^[11].

Potential occupational restrictions include medical and surgical complications, such as risk for hypoglycemia with post-transplant diabetes, and infection susceptibility secondary to immunosuppression. However, "hard data" are lacking. The American Society of Transplantation Infectious Diseases Community of Practice group^[12] identified risk occupations being working with animals (especially during maximal immunosuppression), health care work, construction work, and outdoors work. Nonetheless, there are few guidelines to guide decisions regarding occupational restrictions, and the group^[12] recommends individualized occupation counseling with the notion that the vast majority of jobs can be made safer by simple measures including vaccination, wearing masks, and reassignment to other duties during periods of intensified immunosuppression.

EMPLOYMENT RATES AFTER LT

Studies from 8 countries (United States, Europe and Taiwan), published after year 2000, have reported employment rates after LT (Table 1). The non-weighted average employment rate in these studies is 37%, ranging from 22% to 55% by study (Table 1). The average employment rate is similar in US and non-US studies: 38% (range 24%-55%) and 37% (range 22%-53%), respectively. A corresponding average rate weighted by study-sample size virtually equals that reported by Huda *et al*^[13] from the United States as this study comprised 21942 patients, more than 11-times the size of the remaining studies combined.

Relevant differences among these studies include the variable time-point of employment assessment relative to LT, patient age distribution, exclusion or inclusion of retirees, mixture of liver-disease etiologies, definition of employment, structure of the welfare system and generosity of disability benefits across countries, and post-transplant rehabilitation measures. Definition of employment lacks standardization and differs in, for instance, the inclusion of full-time vs part-time employment and inclusion of students and homemakers. Moreover, there is paucity of recent data on qualitative aspects of employment: ability to return to the same type of work and income level, and the effects of physical demands of the work. No recent qualitative studies were identified that analyzed pre- to post-transplant changes in ability to perform

Table 1 Employment rates after liver transplantation in studies published after year 2000

Year	Author	Country	Patient number	Employment rate	Mean age (yr)	Follow-up (mo)	Ref.
2014	Weng	Taiwan	106	45%	54	43	[16]
2012	Huda	United States	21942	24%	-	< 24	[13]
2011	Gorevski	United States	91	38%	56	-	[29]
2010	Duffy	United States	77	35%	-	> 240	[53]
2010	De Baere	Belgium	63	38%	58	-	[14]
2009	Åberg	Finland	353	44%	55	96	[6]
2007	Saab	United States	308	27%	51	52	[17]
2006	Sargent	United Kingdom	60	37%	35	36	[54]
2006	Sahota	United States	105	49%	54	34	[18]
2006	Kirchner	Germany	23	26%	48	62	[55]
2005	Rongey	United States	186	55%	55	41	[15]
2004	Blanch	Spain	126	33%	56	12	[56]
2004	Cowling	United States	152	36%	53	53	[20]
2003	Karam	France	125	53%	51	120	[57]
2001	Moyzes	Germany	103	22%	47	77	[58]

Table 2 Employment rates after kidney transplantation in studies published after year 2000

Year	Author	Country	Patient number	Employment rate	Mean age (yr)	Follow-up (mo)
2014	Tzvetanov	United States	71976	22%		> 12
2014	Nour	Canada	60	38%	49	
2012	Helanterä	Finland	1818	40%	49	84
2012	Eng	United States	204	56%	48	> 24
2012	Chisholm-Burns	United States	75	39%	48	44
2011	Van der Mei	Netherlands	34	67%	51	77
2010	De Baere	Belgium	79	59%	56	
2008	Bohlke	Brazil	272	29%	41-44	35-43
2007	Raiz	United States	411	49%	47	63
2006	Van der Mei	Netherlands	239	52%	50	46
2002	Griva	United Kingdom	347	56%	47	103
2002	Baines	Scotland	49	18%	36	12
2000	Gross	United States	87	30%	40	36
2000	Ostrowski	Poland	80	74%	18-60	47

homemaker or student duties.

EMPLOYMENT COMPARED TO OTHER POPULATIONS

In kidney transplant populations, reported employment rates have varied among studies from 18% to 74%, with the non-weighted average of 46% (Table 2) being somewhat higher than the 37% in LT population studies. A Belgian study comparing employment rates among different transplant types reported the highest rate among recipients of a kidney (59%), followed by heart (44%), liver (38%), and lung (28%)^[14]. All rates fell below the rates in the Belgian general population (62%), but, except for kidney recipients, the rates also fell below those in the general population among persons with functional limitations (handicap or chronic physical or mental illness; 50%)^[14].

It can be argued that this shortfall in employment among transplant recipients may in part be because illness may change a person's values and life priorities, and transplant recipients might therefore decide to participate in other roles that provide them with meaning. Such an effect, however, was not supported

by the findings of De Baere *et al*^[14] who reported similar or lower rates of participation in voluntary work in the transplant population (17.4%) than in the general population (21.5%).

Of note, comparisons of employment with the general population have not been adjusted for social class, education level, or occupation. These limitations notwithstanding, there is a clear discrepancy in that the majority of LTs are performed on working-aged adults during their most productive years, and 87% of recipients reported improved working/functional capacity after LT in one study^[6]; yet, consistently more than 60% of LT recipients do not resume work.

PREDICTORS OF EMPLOYMENT

Various factors with variable definitions have been evaluated for associations with post-LT employment. The most consistent univariate predictors of employment, confirmed in at least 3 independent studies, include young age, male gender, etiology of liver disease, pre-transplant employment, and good functional/health status (Figure 1). Pre-transplant income level, subjective work ability, depression and

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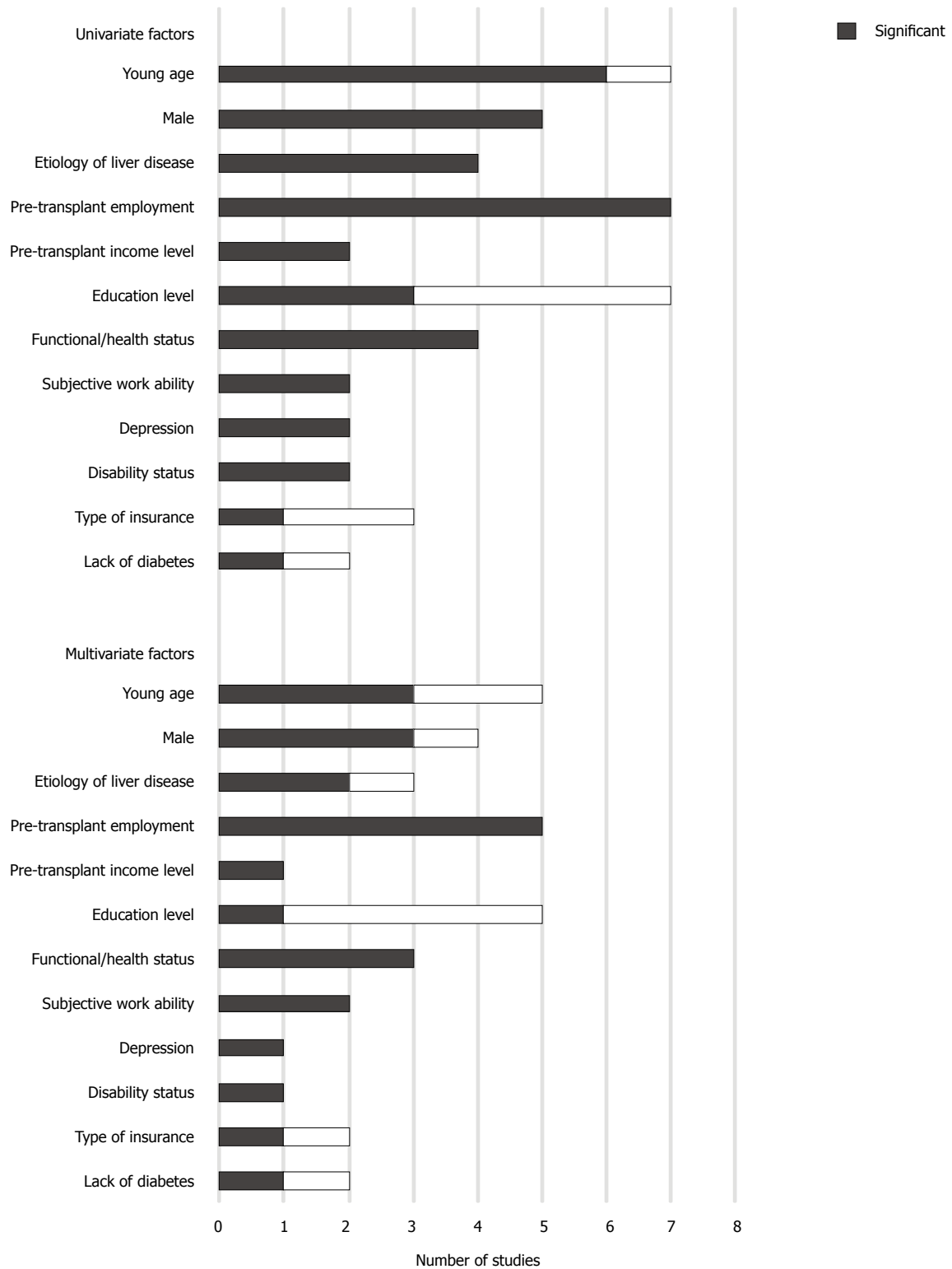


Figure 1 Predictors of employment after liver transplantation. Piles show the number of studies in which the variable was studied, and the dark proportion indicates the number of studies in which the variable was statistically significantly associated with employment. Univariate data are from references^[6,13-18,20,29] and multivariate data from references^[13-17].

disability status were significant predictors in 2 studies each. The influence of education level, type of insurance (in US studies), and presence of diabetes remains controversial (Figure 1).

Few studies performed multivariate analyses, the majority of which are from the United States (Figure 1)^[13-17]. The most robust multivariate data were generated from a US study based on United Network for Organ Sharing data studying employment within 24 mo after LT between 2002 and 2008^[13]; young age, male gender, higher education level, pre-transplant employment, absent alcoholic liver disease, and good functional status emerged as independent positive predictors of post-transplant employment.

Age and gender

In a 2009 Finnish study, more than 80% of recipients aged 20-29 at the time of LT were able to resume work after LT, compared with less than 30% among recipients aged over 50^[6]. Moreover, younger patients were more often able to resume work within 6 mo from the transplant operation^[6]. Being close to retirement age might both decrease willingness to try to resume work and, in some countries, permit disability pension on more lenient grounds. In addition, age-related work discrimination might exist among employers.

Higher employment rates among male recipients may, in part, be explained by the fact that many studies have categorized homemakers as unemployed.

Pre-transplant employment

In multivariate analyses, pre-LT employment emerges as the strongest and most consistent predictor of post-LT employment (Figure 1) with patients employed pre-LT 2.4-7.5-fold more likely to resume work after LT than those unemployed^[13-15]. Moreover, the longer the pre-LT disability period, the lower the likelihood of resuming work^[18]. Sahota *et al*^[18] further reported that patients with "low-skill" jobs were less likely to return to work than were executives, administrators, managers, or technicians.

Liver-disease etiology and severity

Employment rates seem to vary by liver-disease etiology with the highest rates commonly seen among patients transplanted for cholestatic disease (primary biliary cirrhosis and primary sclerosing cholangitis)^[13,19]. Patients transplanted for ALD generally exhibit somewhat lower employment rates than other patients, but this difference is diminishing in recent series^[13] compared to the difference of 33% vs 80% reported by Bravata *et al*^[10] in their 2001 review. Furthermore, such a difference has not been observed in all studies^[15,20], and one series found 2.5-fold higher rates among patients transplanted for ALD compared to primary biliary cirrhosis after adjusting for age^[19].

Few series have analyzed employment among patients transplanted for acute liver failure. In one series^[19] with the acute liver failure group ($n = 76$) comprising a relatively high proportion of young patients (mean age 46 years) and very few intoxications, 61% of recipients were unemployed after LT, and early retirement secondary to disability was the most common reason. This is surprising as patients with acute liver failure are usually healthy and in the workforce before the onset of liver failure rapidly leading to LT. Therefore, patients with ALF emerge as relevant targets for enhanced post-LT rehabilitation efforts.

Severity of liver disease as assessed by the Model for End-stage Liver Disease (MELD) score seems to have no impact on post-LT employment according to US studies^[13,15,17]. In a Finnish series^[21], we observed a drop in post-LT employment rates from 57% at MELD scores < 15 to 36%-39% at higher LT-day MELD scores.

WORK ABILITY AND DISABILITY

Additional employment predictors including functional/health status, subjective work ability, and disability status broadly depict the same concept, namely work ability and disability. From an occupational health perspective, work ability is influenced by individual resources, working conditions, and society (Figure 2)^[22].

Individual resources

In US and Finnish studies, 60%-76% of unemployed LT recipients reported disability or early retirement due to poor health as the cause for unemployment^[6,15,18], but the aspects of health and functional status that impair LT recipients' work ability are incompletely understood. LT patients in the workforce have better health-related quality of life than those unemployed^[6], chiefly attributed to differences in physical health dimensions^[17,23] and fatigue^[23,24].

Fatigue, which affects up to 60% of LT recipients and in its severe form almost half^[24], is more physical fatigue and reduced activity than mental fatigue or reduced motivation^[25]. Fatigue may trigger a vicious circle, leading to inactivity and thus reduction in physical fitness, thereby further increasing fatigue. Fatigue seldom resolves by itself^[26], and no clear association has been found with post-LT medical complications or immunosuppression^[24].

In the general population, depression is a key cause worldwide of long-term disability^[27]. Up to 40% of LT recipients exhibit features of depression, and depressive symptoms are likely underrecognized among LT candidates as well^[28]. Depression has been associated with unemployment and reduced survival after LT^[16,29-32].

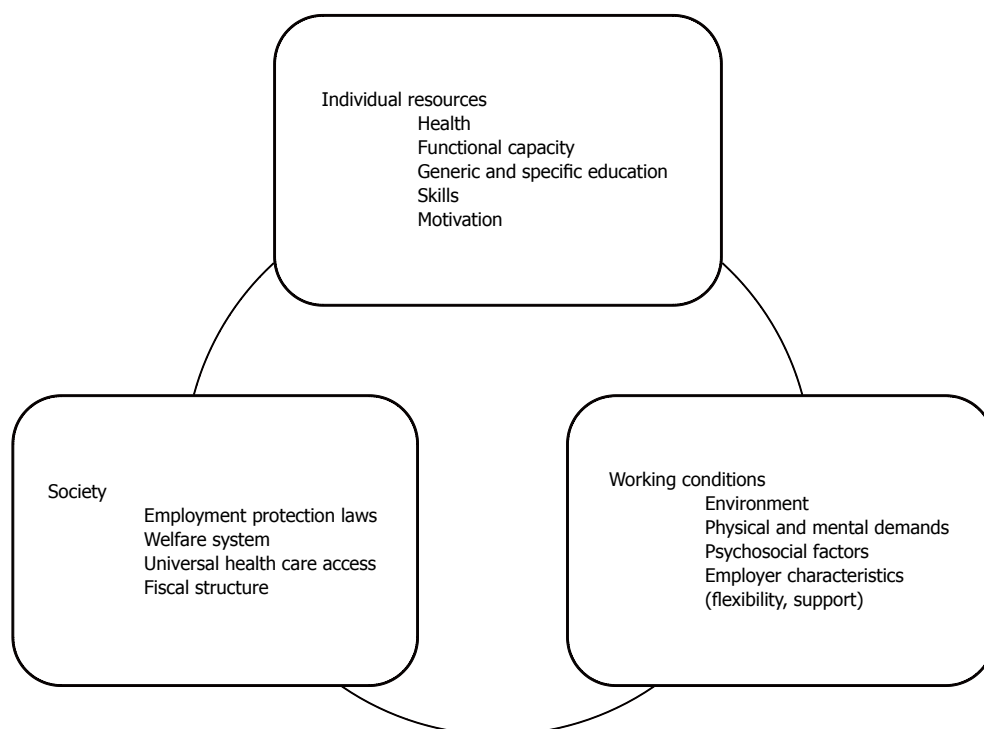


Figure 2 Work ability is a dynamic concept influenced by factors related to individual resources, working conditions and society. Figure constructed based on concepts presented by Ilmarinen *et al*^[22].

Working conditions

In chronic illness and disability, suitable workplace modifications, employer support, and flexible sick-leave practices contribute to participation in paid work in general^[33,34], but specific data for LT populations are scarce. One recent study reported that 58% of LT recipients were fit for the job performed pre-LT, and 74% would have been fit for the job with some work adjustments such as fixed shift or reduced working hours^[35].

Society and socioeconomic aspects

In many countries, disability benefits and early retirement serve to secure financial stability and healthcare access. This is pronounced in the United States, where health insurance is separated in private (usually obtained from the workplace or spouse) and public (*e.g.*, Medicaid). As long-term access to public health insurance is conditional to eligibility for disability benefits or full-age retirement, LT recipients with poor earning prospects and inability to obtain private health insurance may restrain from seeking work and rely on disability income to secure health-care access. In concordance, 12%-20% of unemployed LT recipients in US studies reported they were not working due to fear of losing insurance coverage^[15,18].

Clearly, the concept of post-LT disability extends beyond medical health status, but there are wide differences in pension policies across countries: in the access to benefits, generosity of benefits, and whether

benefits are fixed-term or permanent^[36]. In most countries, however, the annual outflow from disability pension is very low, < 1%^[36]. An exception is United Kingdom with annual outflow around 7%, which is attributed to routine reassessments over time of the entitlement to benefits^[36]. In addition, among disability beneficiaries who exited the benefit (excluding age-retirement), employment rates 3 year later vary from 10% in Germany to 61% in the United Kingdom^[36]. When viewed against these general-population rates, the shortfall in employment among LT patients appears much less pronounced.

STRATEGIES TO PROMOTE POST-LT EMPLOYMENT

Promotion of post-LT employment is hampered by absent interventional studies. Given the variable and individual needs and barriers to resuming work, no single intervention will expectedly benefit all patients. Of the established employment predictors discussed above, pre-LT work ability, post-LT functional status and work ability, fatigue and depression are potentially modifiable and therefore represent targets for employment-promoting interventions.

Pre-transplant work ability

In advanced liver disease, patient work performance may be compromised by liver-related symptoms

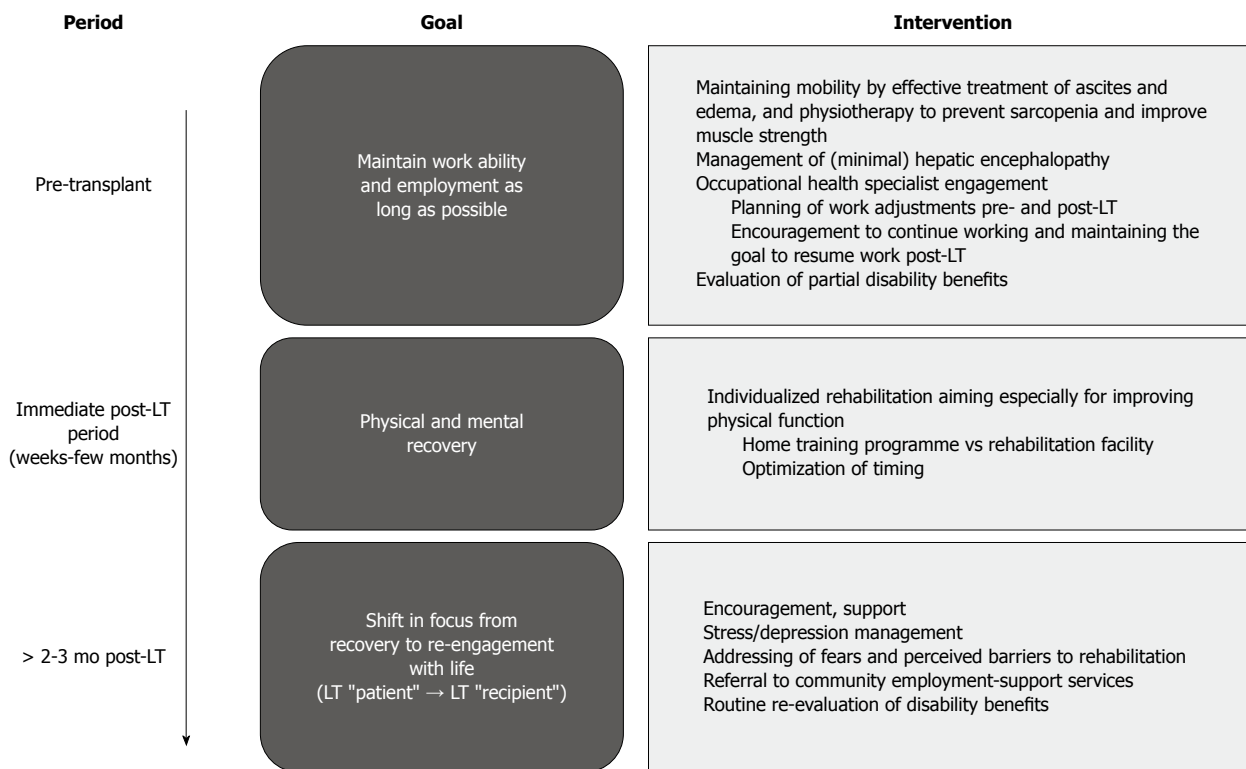


Figure 3 Supporting employment and work ability in the liver transplantation setting - key goals and potential interventions at different time periods.

such as fatigue, covert (minimal) or overt hepatic encephalopathy (HE), and impaired mobility secondary to decreased muscle strength, ascites and edema. Ascites and minimal HE are key drivers of impaired health-related quality of life among nonhospitalized cirrhotics^[37] and features of HE, as assessed by cognitive tests, are independently associated with unemployment^[38]. A Dutch study reported that regular employment was absent in nearly half of cirrhotic patients with minimal HE compared to 15% of patients without minimal HE^[39]. Minimal HE causes impairment in social interaction, alertness, memory, information processing, judgment, sleep, work, home management, and coordination and psychomotor skills such as driving a car^[40]. Recent guidelines^[41] state that neuropsychological testing for minimal/covert HE could be applied to patients with impaired quality of life or implication on employment, and that treatment for minimal HE should be considered on a case-by-case basis. Interventional studies using lactulose or rifaximin have shown high rates of reversal of minimal HE and improvement in both quality of life^[42,43] and driving simulator performance^[44].

Effective control of ascites and edema is important in maintaining mobility, and exercise programs may be beneficial also in advanced liver disease^[45].

Collaboration with occupational-health specialists early in the course of liver disease to plan possible job modifications both before and after LT and to educate

employers about liver disease and LT can help maintain work when the patient later becomes decompensated and a candidate for LT. At this point, partial disability benefits, instead of full disability benefits, may offer the opportunity to retain a job to return to after LT.

Rehabilitation

Early post-LT assessment of needs for physiotherapy is imperative to reverse muscle wasting and deconditioning from the pre-LT period. Patients with strong adaptive capacity might be able to make adjustments independently, whereas those with less adaptive capacity may need assistance, for instance, via dedicated rehabilitation clinics^[46]. Cirrhosis-related hyperdynamic circulation and functional and structural cardiac alterations usually resolve within 6-12 mo post-LT^[47] and risk for incisional hernias secondary to abdominal muscle strains decreases after 6 mo^[11]; these are important considerations for timing of different rehabilitation measures. The most appropriate type of exercise training in transplant recipients has not been well studied^[48]. Preliminary study showed that a 12-wk fatigue-reducing physical rehabilitation program with supervised exercise training and repeated physical-activity counseling sessions was effective in improving severe fatigue and several other aspects of health including questionnaire-based measures of work ability^[49,50]. However, whether rehabilitation efforts truly translate into better work

ability and higher post-LT employment rates remains unproven.

Re-engagement with life

Nour *et al*^[8] interviewed kidney-transplant recipients for their recommendations on how to improve employment. Of respondents, 39% recommended further encouragement from the transplant team, and 57% called for rehabilitation programs with a focus on returning to work^[8]. Screening for and management of depression is also important^[28], as are efforts to increase self-efficacy^[51]. The need for employment-support services available in the community should be assessed in collaboration with social workers.

Countries that target resources towards matching workers with jobs, retraining opportunities and occupational rehabilitation exhibit higher employment rates among chronically ill persons in general^[52].

Health-political discussion is warranted to strive to remove the barriers that require transplant recipients to choose between healthcare coverage and work. Financial encouragements for resuming work while maintaining easy access back to sickness benefits if medical problems ensue have been proposed^[14].

Figure 3 provides a framework of elements at different time periods that, based on current evidence, deserve be incorporated in effective back-to-work programs. Patients transplanted for acute liver failure, those unemployed before LT, and young LT recipients who remain unemployed for 6 mo post-LT emerge as distinct targets for intensified vocational rehabilitation measures. It needs be acknowledged, however, that this framework is not evidence-based, owing to absent interventional studies. As patient needs and barriers to resuming work are highly individual and multifaceted, the contents of back-to-work programs will be difficult to scientifically quantify, and reproducing effective programs at another locale is likely a very challenging task.

CONCLUSION

As an indicator of functional recovery and social re-integration, ability to resume work is becoming a relevant outcome parameter for any transplant center or country to monitor. However, the definition of employment and work needs to be standardized in studies, and the mechanisms behind post-transplant disability are still poorly understood. Although the development and implementation of effective, targeted, and tailored post-transplant rehabilitation and re-integration programs are important unmet research needs, it seems that successful promotion of post-LT employment needs to commence pre-transplant, early in the course of liver disease. Once a potential LT candidate becomes unemployed, the likelihood of being able to return to the workforce after

transplantation decreases dramatically. The concerning fact, found in some healthcare settings, that LT recipients may choose to stay on disability income for fear of losing financial security and healthcare access, calls for a change in policy, to remove the barriers that require LT recipients to choose between healthcare coverage and work. Transplant professionals, social workers and patient organizations can have a key role in initiating such change in policy.

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