

ORIGINAL ARTICLE

EFFECTS OF SMOKING ON LENGTH OF HOSPITAL STAY IN PATIENTS SURVIVING AN ORTHOTOPIC LIVER TRANSPLANT

Shahzad Riyaz, Seema Nadeem*, Anila Riyaz**

Liver Transplant Unit, St James Hospital, UK, *Department of Pathology, Women Medical College, Abbottabad, **Ayub Medical College, Abbottabad, Pakistan,

Background: Smoking in orthotopic liver transplant (OLT) recipients has been associated with increased risk of vascular complications, cardiac events, graft failure and oesophageal cancer. The aim of this study was to determine the effect of smoking on length of hospital stay post OLT and also to audit support provided to these patients. **Methods:** This was a retrospective study carried out in the Liver Transplant Unit, St James University Hospital, UK from 1979 to 2005. One hundred seventy-four 174 adult patients who had undergone OLT in this hospital during this time with a follow-up of at least 2 years after transplantation were included. **Results:** One hundred seventy-four 174 patients (mean age 52.2 years) responded by answering the questionnaire. Answers were analysed using relevant statistical methods. Eighty 80 patients had a smoking history (ever-smoked) while 94 were non-smokers (never-smoked). Out of 56 patients with a smoking history, 46% (n=26) were offered advice and only 18% (n=10) were offered any support. Of the 26 patients smoking at the time of OLT, 58% (n=15) were offered advice and only 19% (n=5) had been offered support. There was no significant difference in length of hospital stay post OLT between patients who had never-smoked and ever-smoked ($p=0.780$). In addition, smoking at the time of OLT had no significant impact on length of hospital stay ($p=0.922$). **Conclusions:** Smoking *per se* does not seem to increase hospital stay post OLT. Patients should be adequately counselled about smoking post OLT. Support mechanisms, including better awareness among doctors and allied healthcare workers should be made available to tackle this problem.

Keywords: smoking, orthotopic liver transplant, OLT

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INTRODUCTION

Orthotopic liver transplantation (OLT) is an accepted therapy for end-stage liver disease. In the last decades, short-term survival after transplantation has improved with nowadays a 1-year survival rate of 85% and a 5-year survival rate of 75%.¹ Besides recurrence of the primary disease, the main causes of death in liver recipients over the long term are cardiovascular events and malignancies. Tobacco use is a well-known risk factor for both.² Therefore, it becomes more and more important to prevent diseases and health problems that are not associated with the original liver disease. Smoking is an important risk factor for cardiovascular events as well as several malignancies. Smoking is considered one of the leading causes of preventable death in the general population and could also be an important one in liver transplant recipients.³

The aim of this study was to determine the effect of smoking on length of hospital stay post OLT and also to audit support provided to these patients. In addition, we looked for a relation between smoking, and survival and morbidity after OLT.

MATERIAL AND METHODS

This was a retrospective study carried out in the Liver Transplant Unit, St James University Hospital, UK between 1979 to May 2005. One hundred and seventy-four adult patients who had undergone OLT in this

hospital during this time with a follow-up of at least 2 years after transplantation were included. These patients were asked to complete an anonymous standardised questionnaire through which data was collected. The immuno-suppression protocol for OLT had been followed by all patients.

From the questionnaire, we collected information about the smoking habits of the patient at 3 time points: before OLT, during evaluation for OLT and shortly before it and 2 years after OLT. The patients were asked about their smoking habits (i.e., active smoker, a former smoker, or never smoked), the number of years of tobacco use or when tobacco use was stopped, on the type of tobacco product, on the average number of cigarettes/cigars per day and on plans for smoking cessation and willingness to have free counselling at the hospital. Smokers were defined as smoking 7 or more cigarettes per week. For converting cigars to cigarettes, we equated 1 cigar with 4 cigarettes, considering that an average cigar contains 4 g of tobacco and an average cigarette contains 1 g of tobacco.⁴

The data were analysed using SPSS. Categorical variables were presented as frequencies with percentages, and continuous variables were presented as medians (range), and $p \leq 0.05$ was considered significant.

RESULTS

One-hundred-seventy-four patients responded by answering most of the questionnaire. Out of these, 80

patients had a smoking history (ever-smoked) while 94 were non smokers (never-smoked). Among the smokers the median pack year history was 13 (range 0.1–56.25). Out of 80 patients with a smoking history, 65 were offered advice and only 15 were offered any support.

For the analysis of the effect of smoking on patient and graft survival, we first had to make comparisons between active smokers and non smokers before and after OLT. There was no significant difference in length of hospital stay post OLT between patients who had never-smoked and ever-smoked. In addition, smoking at the time of OLT had no significant impact on length of hospital stay. Furthermore, no differences were found for the causes of graft failure between smokers and the other patients.

De novo malignancies, excluding skin cancer, developed significantly more often in smokers in comparison with non-smokers. We also found a tendency for hepatic artery thrombosis occurring more often in smokers compared to non-smokers. Tobacco use of patients is given in Table-1 while outcomes after OLT are given in Table-2.

Table-1: Tobacco use from questionnaires (n=174)

Characteristic of patients	No.
Never smokers	94
Smokers	80
Former smokers	25
Active smokers at OLT	55
2 years after OLT	
Actively smoking even after OLT	40
Stopped smoking sometime after OLT	15

Table-2: Outcome for post transplant active smokers and non-smokers

Characteristic	Smokers (n=80)	Non-smokers (n=94)
Re-transplantation	11	28
Hepatic artery thrombosis	19	17
Cardiovascular events <i>de novo</i>	16	12
Hypertension <i>de novo</i>	76	25
Diabetes mellitus <i>de novo</i>	13	34
Malignancies <i>de novo</i>	12	7

DISCUSSION

Long-term morbidity and survival after OLT are determined to a large degree by development of cardiovascular diseases and cancer. Tobacco use is a well-known risk factor for both disease entities. In the UK, discontinuation of tobacco use is encouraged before the actual transplant takes place, but it is not a contraindication. The present study gives us insight into the smoking patterns and OLT. In addition, the study helps to recognise effects of smoking on length of hospital stay in patients surviving an orthotopic liver transplant.

A positive finding was that, of the patients who smoked at the time of the evaluation for OLT, almost one-third succeeded in smoking cessation, often

during the waiting time for OLT. That the overall percentages of active smokers before and after OLT were about the same implies that other patients, mainly former smokers at the time of evaluation, restarted smoking after OLT. We found that especially former smokers who had succeeded in stopping tobacco use a relatively short time. We found that most former smokers started smoking early in their life and quit after a median of 15 years of smoking, long before transplantation. At the end of follow-up, the cumulative number of smoking years was twice as high in the active smokers compared to the former smokers. It was no surprise that almost all patients used tobacco by smoking cigarettes and/or hand-rolling tobacco. Pipes or cigars were enjoyed by only 5% of the patients.

For the analysis of the effect of smoking on patient and graft survival, we first had to make comparisons between active smokers and non smokers before and after OLT via a questionnaire. In the group of 174 patients, 80 responders who reported tobacco use at 2 years after OLT and/or at the end of follow-up were compared with 90 responders who reported abstaining from tobacco use after OLT. No differences were found for patient and graft survival between smokers and non smokers after OLT. Furthermore, no differences were found for the causes of graft failure between smokers and the other patients.

Tobacco use as a risk factor for malignancy after OLT is well recognized.⁵⁻⁷ In the group of survivors who responded to the questionnaire, we did find that the prevalence of non-skin cancer was increased in active smokers after OLT. Tumour types in smokers were cancer of oropharynx, vulva or cervix, colon cancer, and post transplant lymphoproliferative disorder. Tumour types in non-smokers were gastric, colon, and prostate cancer, post transplant lymphoproliferative disorder and hepatocellular carcinoma.

Tobacco use is one of many risk factors for cardiovascular disease after OLT. Other risk factors include raised BMI, diabetes, hypertension, and use of immunosuppressive agents. We found a tendency for hepatic artery thrombosis occurring more often in smokers compared to non-smokers.^{8,9} The PSC group is remarkable with 1.4% being active smokers and 77% being never smokers at the time of evaluation for OLT.

Tobacco use was highest in patients with ALD and in those with acute liver failure. During the evaluation, 52% of the alcoholic group were active smokers (and only 8% were never smokers). The combination of alcohol and tobacco addiction is well known and has been reported to be as high as 90% in alcohol abusers.^{10,11} Since alcohol abstinence for at least 6 months is a prerequisite for OLT in the UK, it is disturbing that so many still continued active smoking. DiMartini *et al.* from Pittsburgh reported tobacco use after OLT for ALD patients to be an underestimated

problem as these patients were reported to have a high incidence of lung and pharyngeal cancer.¹²

There are very few studies in liver transplant patients reported. Ehlers *et al*¹³ studied patients transplanted in Florida. Their method was a structured interview by telephone with a 42% response rate. They reported an active smoker rate of 15% after OLT and a relapse rate of 20% in former smokers. From both studies, it follows that intervention programs should be aimed not only at active smokers but also at former smokers and that these programs should be continued for many years, if not for the rest of their lives.

This study confirms that smoking should not be a contraindication to liver transplant as smoking does not seem increasing hospital stay after OLT. There is an increased risk towards malignancies and hepatic artery thrombosis in active smokers. Therefore, patients should be adequately counselled about smoking post OLT. Pretransplant intervention programs should be aimed not only at active smokers but also at former smokers, especially those who stopped smoking recently. The higher prevalence of malignancies in active smokers after OLT warrants intervention programs after OLT and regular screening for malignancies.

CONCLUSION

This study would suggest that smoking should not be a contraindication to liver transplant as smoking does not seem to increase hospital stay after OLT. Other studies have shown an increased risk towards malignancies and hepatic artery thrombosis in active smokers. Patients should therefore be adequately counselled about smoking post OLT. Awareness amongst doctors and patients should be developed to manage this issue.

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Address for Correspondence:

Dr. Shahzad Riyaz, Consultant Hepatologist/Gastroenterologist, Barnsley Hospital, NHS Foundation Trust, Barnsley, UK.

Email: drsrq@hotmail.com