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A questionnaire based assessment of numbers, motivation and medical care of UK patients undergoing liver transplant abroad

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Summary *Background:* Medical tourism, where patients travel abroad intentionally to access medical treatment, is a growing trend. Some of these patients travel to undergo organ transplantation. This study aims to quantify the number of UK patients who undergo liver transplantation abroad, assessing their motivations and management.
Methods: Questionnaires were sent to all seven UK liver transplant units enquiring about liver patients receiving transplant abroad. Included were questions on destination, motivation, and pre and post-transplant care.
Results: Responses were received from six of the seven transplant centres (86%). A total of 12 patients were identified as having undergone liver transplantation overseas. The top destinations were India, China and Egypt. Four units responded to questions regarding pre-transplant screening. One unit reported Hepatitis B and C screening not taking place. Four units responded to questions regarding post-transplant antimicrobial therapy. This revealed examples of patients inappropriately not receiving valganciclovir, co-trimoxazole, anti-fungal treatment and Hepatitis B immunoglobulins.
Conclusions: UK patients are undergoing liver transplant abroad, albeit in small numbers. Pre and post-transplant management of these patients is of a lower standard than that provided to those undergoing transplantation in the UK. Information transfer between overseas and UK based transplant teams is poor.

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1. Introduction

Liver transplant is a treatment option for patients with end stage liver disease arising as a result of a range of acute and chronic pathologies [1]. In March 2015 there were 611 patients, 566 of them adult, awaiting liver transplant in the UK, an increase from 371 in 2010 [2]. There is accordingly an unmet demand in the UK liver transplant system.

Median waiting time for adult elective patients is 152 days. However, two years after joining the transplant list, 13% of patients have either died before they could be transplanted or have been removed from the list due to irretrievable deterioration in their health. Furthermore, 4% of patients wait longer than two years for a transplant [2].

It has become increasingly common for patients to seek healthcare abroad, for a variety of reasons. This phenomenon is commonly known as 'medical tourism', and is a world-wide phenomenon. Reliable quantitative data on the overall scale of medical tourism are difficult to obtain, and estimates vary significantly, but it is generally accepted that medical tourism is a growing trend [3]. A specific subset of medical tourism is 'transplant tourism'. Typically this involves patients from higher-income countries travelling to lower-income countries for organ transplantation, although the patterns of flow between different countries do change with time [4].

As these transplants occur outside of the UK, and hence not within the National Health Service (NHS), patients may not be subject to the same routine pre- and post-transplant care that would be expected for UK NHS patients. The geographical distance between patients' normal residence and the transplant hospital can also make pre and post-transplant care more challenging. Both of these factors may lead to sub-optimal standards of care.

This paper attempts to quantify the levels of UK patients travelling abroad for liver transplant. It aims to assess the adequacy of pre and post-transplant care, and also to investigate the motivations behind seeking liver transplantation overseas. The methodology used in this study is based on similar research into renal transplant tourism carried out by two of the authors of this study [5].

2. Methods

The study methodology was a cross-sectional survey using an online questionnaire. Data collected between 27th November and 15th December 2015. A senior clinician at each of the UK's seven liver transplant centres (six in England, one in Scotland) was identified through their online staff directories, or by a telephone call to the department. These were either consultant liver transplant surgeons or consultant hepatologists working in the liver transplant field. The clinicians were then invited to complete the survey on behalf of their liver transplant unit.

The survey included questions about the number of patients known to the unit who had received transplant overseas, along with what was known about their destination and motivation. It also included questions about these patients' pre and post-transplant medical management and counselling. As there are no UK national-level guidelines that cover this currently in existence, the questions asked were informed by a review of liver transplant guidelines from two NHS centres (one in Scotland [6–8], one in England [9]) and the USA (American Association for the Study of Liver Disease [10,11]) to ascertain routine practice in advanced Western health systems.

As this study aimed to ascertain the experiences and opinions of doctors, and did not involve approaching patients individually or obtaining patient identifiable data, it was not deemed necessary to seek ethical approval. In order to maximise response participation, clinicians were not obliged to respond to all questions. Consequently, some questions had lower response rates than others.

3. Results

Clinicians from 6 out of the 7 UK liver transplant units responded (86%), 5 through our survey and 1 by free-text email. Where results are reported by centre, centres have been anonymised to numbers ranging 1 to 6.

3.1. Destination and motivation

Four out of the six responding units had patients who travelled abroad for transplant surgery (67%). One unit had one patient, two had two patients, and one unit had seven patients. The unit with the highest number of patients undergoing transplant abroad was located in London. The top destinations were China, Egypt and India, with three patients having had surgery in each. Other destinations were South Africa, France and the USA, each represented by a single patient. Two patients had liver transplants whilst they were resident in another country. One had a transplant abroad in order to shorten the time they spent waiting for surgery to take place. Eight patients did not meet eligibility criteria for the UK liver transplant register. The reason for ineligibility was not recorded.

3.2. Health advice

Four out of six units (67%) responded to questions regarding post-operative health advice given by the overseas transplant team. One unit reported that patients had been given advice regarding protection from solar exposure and avoidance of live attenuated vaccines. One unit reported that patients had not been given any such advice, whilst two units did not know.

3.3. Pre-operative screening

Four out of six units (67%) responded to questions about pre-operative screening for Cytomegalovirus (CMV), Epstein–Barr virus (EBV), Varicella Zoster virus (VZV), Hepatitis B virus, Hepatitis C virus and Carbapenemase Producing Enterobacteriacae (CPE). The results are shown in Table 1. One unit reported that one patient had not been screened for Hepatitis B and C viruses, but did not know about the other pathogens. The three other units did not know what pre-operative screening the patients had undergone.

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Table 1 Proportion of patients screened for evidence of pathogens before surgery, by centre (n = 4).

	Centre number			
	1	2	3	5
CMV	u	u	u	u
EBV	u	u	u	u
VZV	u	u	u	u
Hep B	None	u	u	u
Hep C	None	u	u	u
CPE	u	u	u	u

Note: u = unknown, CMV = Cytomegalovirus, EBV = Epstein–Barr Virus, VZV = Varicella-Zoster Virus, Hep B = Hepatitis B Virus, Hep C = Hepatitis C Virus, CPE = Carbapenemase Producing Enterobacteriaeace.

3.4. Intra and post-operative management

Four out of six units (67%) responded to questions about intra-operative and post-operative anti-microbial therapy. The results are shown in Table 2. One unit confirmed that their patients had not received indicated co-trimoxazole. One unit reported that their patients had not received an indicated anti-fungal agent. Two units reported that their Hepatitis B positive patients had not received indicated anti-HBs immunoglobulins. One unit reported that their patients had not been started on indicated valganciclovir.

3.5. NHS approach to prospective transplant tourists

Five out of six units (83%) responded to a question about advance notice of intention to obtain liver transplant abroad. Only one unit had received advance notice, and only on a single occasion. Four units responded to a question about counselling in the UK for patients giving advance notice of intention to undergo transplantation abroad. None of these units have a formally organised service in place to deal with queries of this type from patients.

Five units responded to questions about written policies for liver transplant. Four out of five units (80%) reported having a written policy dealing with liver transplants occurring in the UK. None of the five currently have a written policy for dealing with any forthcoming transplants being organised abroad by a patient themselves or by their relatives/friends.

Table 2 Proportion of patients starting indicated intra-operative and post-operative management, by centre (n = 4).

	Centre number			
	1	2	3	5
Intra-operative co-amoxiclav	u	u	u	u
Intra-operative and early anti-HBS	None	None	u	u
Co-trimoxazole	u	None	u	u
Anti-fungal	u	None	u	u
Valganciclovir	u	None	u	u

Note: u = unknown, anti-HBS = anti Hepatitis B Virus immunoglobulins.

4. Discussion

This survey approached, and received feedback from, virtually all of the services currently providing liver transplantation in the UK. The results of the survey suggest that liver transplant tourism does occur in the UK, although on a small scale, with significant variation in numbers between different units. In the majority of cases UK clinicians are not informed in advance of a patient's intention to undergo transplantation abroad. The transfer of information between the clinicians performing the transplant abroad and the UK liver transplant team is poor. There is very limited information known about the pre-operative screening and post-operative anti-microbial therapy that these patients receive. The little information available suggests sub-optimal management.

This study identified 12 cases of patients under the care of UK liver transplant teams who underwent liver transplant abroad. Given that 690 adult liver transplants were performed in the UK in the 2014/2015 financial year alone, this represents a tiny proportion of the total UK liver transplant population [2]. This study did not seek to explore the variation in number of patients undergoing transplant abroad between different liver transplant units. However, we hypothesise that the ethnic make-up of each unit's catchment population may be a determinant. In support of this London, the most ethnically diverse region of the UK, saw a disproportionately high number of liver transplants performed overseas.

The study demonstrates poor transfer of information regarding a patient's pre and post-operative management from the team performing the transplant to the patient's UK transplant team. This has been identified as a major problem in small case-series of American and Australian patients receiving kidney transplant abroad — a more thoroughly studied transplant procedure [12]. We assume that after discharge from the overseas hospital, the majority of patients will then return to their UK based transplant team for routine follow-up and for all emergency care. Incomplete information transfer increases the risk to the patient post-operatively as doctors are then obliged to make management decisions without being in possession of a complete record of prior treatment. The potential complications of any suboptimal patient management abroad are likely to be managed in the NHS and funded by UK taxpayers.

Where information is known about pre and post-operative management of transplant patients abroad, it suggests suboptimal care. The one patient for whom screening information was available had not been screened in advance of surgery for viral hepatitis, a major cause of liver disease. Screening for viral hepatitis should be obligatory in every liver transplant case. The study also identified cases where valganciclovir, anti-fungals, co-trimoxazole, and anti-HBs immunoglobulins should have been given but were not. Valganciclovir is effective prophylaxis against CMV [11]. Co-trimoxazole is used as

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prophylaxis against *P. jirovecii*, an infection risk in immunosuppression, whilst anti-HBs immunoglobulins are highly effective at preventing re-infection in liver transplant for hepatitis B [13,14]. The under-use of effective post-operative prophylaxis mirrors what two of the authors found in a previous study examining renal transplant tourism [5]. A review by Chen and Wilson of infectious disease transmission to medical tourists identified multiple cases of infection from donor organs and blood, likely a consequence of poor standards similar to those we have found [15].

A meta-analysis of outcomes following kidney transplant abroad identified an increased risk of contracting CMV, hepatitis B, HIV and wound infections compared to domestic transplant [13]. The sub-optimal anti-microbial therapy practices identified in this study suggests that infection risk following liver transplant may also be higher when the operation is performed outside of the UK. Outcome data on UK patients who underwent liver transplant abroad were not collected in this study, but could potentially be analysed in the future. There are also no data available on the health status of the donors, either pre or post-transplant. This data would likely be very difficult if not impossible to obtain and would raise ethical issues with regards to the recipients' knowledge of their donor's health and hence around genuinely informed consent. Therefore, we did not enquire about pre-transplant screening of the organ donor in this survey.

The source of donor organs raises ethical and legal questions about the practice of transplant tourism [16]. There has been far greater investigation into transplant tourism for kidneys than for livers. The research suggests that many kidneys are purchased from unrelated living donors, typically from lower-income individuals [14,17,18], whilst it has been reported that persons subjected to capital punishment may account for the majority of donor organs in China [19]. Research from India has shown that a commercial-based kidney donation system frequently results in a deterioration in health of the donors that over time can outweigh the short-term financial reward arising from selling a kidney [14]. These concerns and others have led the World Health Organisation to recommend states ban the sale of donor organs for profit [20]. A number of countries have passed laws to ban the transplant of organs from unrelated living donors to foreigners, including India and Pakistan, although reports of illegal sales persist [21].

The majority of patients identified in this study obtained liver transplant abroad because they were not eligible for the UK transplant register. Consequently patients with end-stage liver disease who are ineligible for the UK transplant register should be considered a high-risk group for obtaining liver transplant abroad. An argument could be made that patients in this group should be provided with expert-led counselling regarding the medical, legal and ethical aspects of seeking out and undergoing liver transplantation abroad. Currently it is not known if it is part of the routine work-up to ask patients if they are contemplating becoming transplant tourists, and this survey did not seek this information.

There are limitations to this study. Whilst survey responses were received from 6 out of 7 liver transplant units (86%), not all respondents answered all of the questions. Some questions were only responded to by 4/6 responding units, a response rate of 66%. Survey respondents (who were senior consultants) were asked to provide information on behalf of their whole unit, but their knowledge of cases under the direct care of a different consultant may be incomplete. Consequently the total number of overseas liver transplants counted in this study may be an underestimate. Similarly, detailed information regarding pre and post-transplant management of each case may be known by the patient's responsible consultant but not by the survey respondent. As a result we may have inferred a poorer level of information transfer between overseas and UK transplant teams than is actually the case.

5. Conclusion

This is the first study of its kind attempting to quantify the number of UK NHS patients undergoing liver transplant abroad, as well as investigating their motivations and the standards of pre and post-transplant care. It is clear that although the numbers are small, most UK liver transplant units provide post-operative and ongoing care to patients who have undergone transplantation abroad. The management of these patients by the overseas team appears to be in general of a lower standard than what would ordinarily be provided in the UK. Further study is needed to compare the outcomes for these patients with those who undergo their entire transplant process in the UK.

A case could be made for end stage liver failure patients being asked proactively about their future plans (if any) in relation to whether or not they are considering medical tourism as an option. If they are considering it, then this may allow for intervention to be put in place, for example the provision of expert counselling for those who are ineligible under current guidelines for a UK-based liver transplant. This should cover the risks, ethics and legality of transplantation abroad. Such counselling may raise a number of ethical issues for UK healthcare workers charged with looking after these patients and who have a duty to help them — for example, will mentioning transplant tourism to a patient implant an idea in their mind that they had not considered up till then? Or would taking such a view be unacceptably paternalistic? This definitely merits further debate and discussion.

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Contributions

BKW wrote the questionnaire, corresponded with respondents, analysed the results and prepared a first draft of the manuscript. SG and AO designed the study, reviewed the questionnaire and manuscript drafts and provided supervision and guidance to BKW. All authors reviewed and approved the final draft of the manuscript.

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Conflict of interest

We have read, understood and signed the Travel Medicine and Infectious Disease conflict of interest statement and declare that we have no competing interests.

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