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Original article

Invasive coronary angiography as a tool in cardiac evaluation for liver transplant candidates

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ABSTRACT

Background: Cardiovascular assessment is central to evaluation of liver transplant (LT) candidates. However, there is a lack of consensus on the diagnostic algorithm for screening for coronary artery disease (CAD), and the place for invasive coronary angiography (ICA) remains undefined.
Methods: We retrospectively analysed 1201 adults who underwent elective LT assessment over a 5-year period. For patients who underwent LT, survival data to 5 years post-LT was collected.
Results: ICA was performed in 259 (21.6%): 134 no CAD, 58 mild, 33 moderate, and 34 severe. Detection of CAD was associated with age (OR 1.08, $P < 0.01$), current smoking (OR 4.92, $P < 0.01$) and prior CAD (OR 8.93, $P < 0.001$). Poor performance on cardiopulmonary exercise test (CPET) was associated with age (OR 1.02, $P < .05$) and diabetes mellitus (OR 1.54, $P < 0.05$). 122 (10.2%) patients were declined due to severity of cardiovascular disease.
169/779 (21.7%) patients listed for LT had undergone ICA, and CAD was present in 73/169 (43.2%). The non-risk-adjusted all-cause post-LT 5-year survival was 82.6%, with no difference in survival in those with and without CAD on ICA. In patients with CAD, diabetes was associated with reduced survival (OR 3.78, $P < 0.05$).
Conclusions: Multi-modality cardiac evaluation is useful in high-risk patients undergoing LT assessment. ICA can be used with non-invasive assessments and risk factors to delineate candidacy. In selected patients with CAD, LT has been undertaken with comparable post-LT survival.

1. Introduction

Evaluation for liver transplantation (LT) is a multi-disciplinary process where the risk-benefit for an individual proceeding with LT needs to be carefully considered [1]. An accurate cardiovascular assessment is crucial to determine whether individuals can survive the peri-operative period and also whether sufficiently severe disease exists to exclude patients from LT [1,2]. There is a significant prevalence of coronary artery disease (CAD) in LT candidates, which is often asymptomatic even in the presence of moderate CAD [3].

Abbreviations: AT, anaerobic threshold; CAD, coronary artery disease; CPET, cardiopulmonary exercise test; ECG, electrocardiogram; ICA, invasive coronary angiogram; LT, liver transplantation; MELD, model for end-stage liver disease; NAFLD, non-alcoholic fatty liver disease; PCI, percutaneous coronary intervention; TTE, transthoracic echocardiogram; UKELD, United Kingdom model for end-stage liver disease

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Identifying which LT candidates to screen for silent CAD and which diagnostic tools to employ are clinical challenges without clear answers [4]. Guidelines recommend initial assessment with electrocardiogram (ECG) and transthoracic echocardiogram (TTE) [1,2], however when to proceed with non-invasive testing differs between centres. Dobutamine stress echocardiography in all patients [1], and non-invasive stress testing based on the presence of cardiovascular risk factors has been proposed [2,5,6]. The lack of a consensus and the limitations of non-invasive stress testing in patients with end-stage liver disease [3,4] contribute to the wide variation seen in clinical practice.

More recently, screening with invasive coronary angiography (ICA) has been included in recommendations in those with a high pre-test probability based on risk factor profile [6]. Although ICA can be safely used in patients with end stage liver disease [6,7], due to the potential complications it is only recommended in selected individuals. Using a risk factor based protocol approach to ICA in LT candidates identifies significant CAD disease in a proportion of patients [3,8]. In the time periods since protocolised ICA has been introduced an improvement in post-LT cardiovascular morbidity and all-cause mortality has been described [9]. In LT candidates identified with CAD on ICA who were carefully selected and managed appropriately, there appears to be reasonable post-LT outcomes [10–12].

The aims of our study are to describe our experience of cardiac evaluation of LT candidates using non-protocolised ICA in combination with non-invasive tools, and to report the long-term outcomes of patients who underwent LT with evidence of CAD on ICA pre-LT.

2. Patients and methods

Patients assessed for LT at King's College Hospital were identified from a prospectively collated electronic database. A retrospective analysis of electronic patient records and paper notes was performed on all patients aged 18 or over assessed for LT over a 5 year period (2007–2011). Patients with acute liver failure syndromes were excluded. This was performed as an audit in accordance with the ethical standards laid down in the Declaration of Helsinki 2013 and the Declaration of Istanbul 2008.

Baseline data collection included demographics, clinical characteristics, biochemical and haematological results, and details of cardiac investigations. Assessment of suitability for LT was performed by members of the transplant team and was in accordance with guidelines. Standard cardiac assessment included electrocardiogram (ECG), transthoracic echocardiogram (TTE) and cardiopulmonary exercise test (CPET). Based on an individual's risk factors and performance on these non-invasive tests, a decision was made to proceed with invasive coronary angiography (ICA).

2.1. Outcome measures

All cases were discussed in the LT multi-disciplinary meeting where a decision was made to either list or decline for transplantation. The outcome of the meeting was recorded, including the reasons for decline. Date of transplant was recorded, and for patients who underwent LT, post-transplant mortality data was collected.

2.2. Definitions

CPET: Poor performance on CPET was defined by one of: anaerobic threshold (AT) < 9 mL/Kg/min, AT not achieved, or ECG changes occurring during CPET.

ICA: Presence of coronary artery disease on ICA was defined as >= 20% stenosis in a major vessel. Degree of stenosis was classified into: mild – 20–49% stenosis; moderate - 50–69% stenosis; severe - 70 –99% stenosis or total occlusion of vessel.

Cardiovascular risk factors: A personal history of ischaemic heart disease (myocardial infarction, PCI and/or coronary artery bypass graft), diabetes mellitus, hypertension, non-alcoholic fatty liver disease and smoking history (current or ex-smoker). An ex-smoker was defined as having not smoked for at least 28 days. The total number of risk factors was calculated for each patient.

2.3. Statistical analysis

Analyses were undertaken on the statistical software StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC. A p-value < 0.05 was considered statistically significant. A multivariable logistic regression model was developed to assess factors associated with performing poorly on CPET, factors associated with CAD on ICA and factors associated with all-cause five-year mortality among patients with CAD. For mortality outcomes, a complete case analysis was used. Data was assumed missing at random. Variables of interest between the two groups were comparable. Characteristics of patients undergoing coronary angiography who were listed for LT were completed using Chi-squared tests for categorical data and unpaired *t*-test for means.

3. Results

3.1. Cohort characteristics

In total, 1201 patients underwent LT assessment between 1 January 2007 and 31 December 2011. The cohort characteristics are shown in Table 1. Median age at the start of the assessment was 55 (17–75) years and 807 (67.2%) were male. The predominant aetiology of liver disease was alcohol, in 347 (28.9%) of potential transplant candidates. Severity of liver disease was recorded using the Model for End-stage Liver Disease (MELD) and United Kingdom Model for End-Stage Liver Disease (UKELD) scores. The mean MELD score was 15.4 (SD 6.4) and the mean UKELD 54.4 (SD 5.7). Cardiovascular risk

Table 1
Characteristics of patient cohort undergoing liver transplant assessment.

Variables		Whole cohort (*n* = 1201)
Sex	Male (%)	807 (67.2)
	Female (%)	394 (32.8)
Age (years)	Mean (SD)	55 (17-75)
Aetiology	Alcohol (%)	347 (28.9)
	HCV (%)	180 (15.0)
	Other (%)	147 (12.2)
	Mixed (%)	99 (8.2)
	PBC (%)	85 (7.1)
	NASH (%)	75 (6.2)
	HBV (%)	74 (6.2)
	PSC (%)	73 (6.1)
	Cryptogenic (%)	64 (5.3)
	AIH (%)	57 (7.4)
UKELD	Mean (SD)	54.4 (5.7)
MELD	Mean (SD)	15.4 (6.4)
CAD	Yes (%)	93 (7.7)
	No (%)	1108 (92.3)
HTN	Yes (%)	204 (17.0)
	No (%)	997 (83.0)
DM	Yes (%)	323 (26.9)
	No (%)	878 (73.1)
NAFLD	Yes (%)	84 (7.0)
	No (%)	1117 (93.0)
Smoking	Non (%)	569 (47.4)
	Ex (%)	439 (36.6)
	Current (%)	190 (15.8)

Abbreviations: HTN, hypertension; DM, diabetes mellitus; NAFLD, non-alcoholic fatty liver disease; CAD, coronary artery disease; MELD, Model for End-stage Liver Disease; UKELD, United Kingdom Model for End-Stage Liver Disease.

Table 2
Non-invasive assessment of cardiovascular disease. * Poor performance on CPET was defined by one of: anaerobic threshold (AT) < 9, AT not achieved, or ECG changes occurring during CPET.

Variables		Whole cohort (*n* = 1201)
ECG (ischaemia)	Normal (%)	1103 (91.8)
	Ischaemia (%)	79 (6.6)
	Not performed (%)	19 (1.6)
ECG (rhythm)	Normal rhythm (%)	1129 (94.0)
	Abnormal rhythm (%)	53 (4.4)
	Not performed (%)	19 (1.6)
TTE (RWMA)	Normal (%)	1146 (95.4)
	Motion abnormality (%)	41 (3.4)
	Not performed (%)	14 (1.2)
TTE (LV function)	Normal (%)	1158 (96.4)
	Impaired (%)	29 (2.4)
	Not performed (%)	14 (1.2)
CPET performance*	Satisfactory (%)	503 (41.9)
	Poor (%)	176 (14.6)
	Not performed (%)	522 (43.5)

Abbreviations: RWMA, regional wall motion abnormality; TTE, transthoracic echocardiogram; CPET, cardiopulmonary exercise testing; ECG, electrocardiogram; LV, left ventricle.

factors, as defined by ischaemic heart disease, diabetes mellitus, hypertension, non-alcoholic fatty liver disease and smoking history were recorded. In total, 111 (9.2%) had ≥3 risk factors, 216 (18.0%) had 2 risk factors and 534 (44.5%) had 1 risk factor.

3.2. Non-invasive cardiac assessment

Non-invasive assessment of cardiovascular disease consisted of a baseline ECG, TTE and CPET. In our patient cohort, 79 (6.6%) had evidence of ischaemia and 53 (4.4%) had evidence of an arrhythmia on the baseline ECG. Only a small proportion had evidence of regional wall motion abnormalities (41/3.4%) and left ventricular dysfunction (29/2.4%) on echocardiogram (Table 2).

CPET is used as the main non-invasive cardiovascular assessment at our centre. CPET was not performed in 522 (43.5%) patients due to a multitude of factors including availability of CPET, inability to attempt the CPET (e.g. pain, encephalopathy) or adequate fitness deemed by clinical assessment. Factors associated with performing poorly on CPET were age (OR 1.02; $p < 0.05$) and diabetes mellitus (OR 1.54; $p < 0.05$) (Table 3).

3.3. Invasive coronary angiography

Presence of multiple cardiovascular risk factors and performance on CPET were used to decide on the need for invasive cardiac assessment using ICA. In total, 259 (21.6%) patients underwent ICA. The average number of risk factors in this group was 1.9, compared to 0.9 for patients not undergoing ICA. Among patients who did not undergo ICA, 44/943 (4.7%) had ≥3 risk factors, 134/943 (14.2%) had 2 risk factors, and 442/943 (46.9%) had 1 risk factor.

Table 3
Factors associated with poor performance on CPET. Poor performance on CPET was defined by one of: anaerobic threshold (AT) < 9 mL/Kg/min, AT not achieved, or ECG changes occurring during CPET.

Variables		OR	CI (95%)	*p* value
Age		1.02	1.01–1.04	**<0.05**
Gender		0.71	0.48–1.05	0.09
Smoking	Ex-smoker	1.19	0.79–1.77	0.41
	Smoker	1.38	0.83–2.28	0.21
HTN		0.61	0.37–1.0	**<0.05**
DM		1.53	1.02–2.30	**<0.05**
NAFLD		1.52	0.80–2.87	0.20
CAD		1.23	0.67–2.28	0.50
LV dysfunction		2.60	0.88–7.61	0.08

Abbreviations: HTN, hypertension; DM, diabetes mellitus; NAFLD, non-alcoholic fatty liver disease; CAD, coronary artery disease; LV, left ventricular; CPET, cardiopulmonary exercise testing.

Table 4
Factors associated with presence of CAD at ICA.

Variables		OR	CI (95%)	*p* value
Age		1.08	1.03–1.13	**<0.01**
Gender		1.40	0.63–2.97	0.43
Smoking	Ex-smoker	1.16	0.59–2.26	0.66
	Current smoker	4.92	1.80–13.42	**<0.01**
HTN		1.24	0.63–2.43	0.53
DM		1.29	0.68–2.44	0.44
NAFLD		0.95	0.39–2.29	0.91
Known CAD		8.93	4.40–18.15	**<0.001**

Abbreviations: HTN, hypertension; DM, diabetes mellitus; NAFLD, non-alcoholic fatty liver disease; CAD, coronary artery disease; LV, left ventricular; CPET, cardiopulmonary exercise testing.

Among the 259 who underwent ICA, 134 (51.7%) had no evidence of CAD, 58 (22.4%) mild CAD, 33 (12.7%) moderate CAD and 34 (13.1%) severe CAD. A multi-disciplinary decision for revascularisation was taken on an individual case basis, and was based on factors including flow limiting lesions, number of vessels, bleeding risk on anti-platelet therapy, overall transplant candidacy, and futility. Percutaneous coronary intervention (PCI) was completed in 13 patients. Of those undergoing PCI, two were declined for LT. In 3 patients CABG at time of LT was recommended. Table 4 shows the factors associated with presence of CAD at ICA, which included age (OR 1.08; $P < 0.01$), current smoking (OR 4.87; $P < 0.01$) and prior history of CAD (OR 8.80; $P < 0.001$).

3.4. Outcome of LT assessment

Following LT assessment, 779 patients were listed for transplant, 388 were declined and 34 patients died before a final decision could be made. Among those declined, 122 (31.4%) were due to cardiovascular disease with 55 (44.7%) of these patients undergoing ICA. Clinical judgement was used at the transplant meeting to decide whether to decline patients for LT based on cardiovascular disease taking into account number of risk factors, severity of CAD at ICA and whether PCI was technically possible.

Among those listed for transplant, 169 underwent ICA with 96 (56.8%) having no CAD, 38 (22.5%) mild CAD, 19 (11.2%) moderate CAD, 16 (9.5%) severe CAD and 11 (6.5%) underwent PCI. Fourteen patients listed for transplant had ≥3 risk factors but did not undergo ICA as part of their risk assessment. Among these, 9 (64.3%) had a satisfactory CPET result, 3 did not undergo CPET and 2 had a poor CPET result. Both of these were non-smokers with no previous history of CAD and the plan had been for a repeat CPET: one did not improve their AT but their general performance on CPET did improve; and the other patient died prior to repeat CPET.

Table 5 gives a comparison between patients undergoing ICA who were listed and who were declined. Patients who were smokers, had previous history of CAD or had evidence of CAD at ICA were less likely to be listed for transplantation. There was no significant difference among patients who underwent PCI.

3.5. Post LT outcomes

Of the 1201 patients assessed, 578 underwent liver transplant, 107 died on the list and 94 were de-listed. The non-risk-adjusted all-cause post-transplant five-year survival was 82.58% (missing data from 90 patients predominantly due to care being transferred to another centre). There was no significant difference in mortality among patients with any degree of CAD identified at ICA compared to those with no CAD (Supplementary Table 1). We subsequently looked at factors associated with all-cause five-year post-transplant

Table 5
Characteristics of patients undergoing coronary angiography who were listed for LT. * analysed using chi-squared test except for mean data that used unpaired T test ($p < 0.05$ considered statistically significant).

Variables		Non-listed (n = 90)	Listed (n = 169)	Odds ratio (P value)*
Age (years)	Mean (SD)	59.8 (7.2)	58.1 (7.4)	**(<0.001)**
Sex	Male (%)	72 (35.0)	134 (65.0)	0.96 (0.89)
	Female (%)	18 (34.0)	35 (66)	
Smoking	Non (%)	30 (28.8)	74 (71.2)	**0.74 (<0.001)**
	Ex (%)	35 (29.9)	82 (70.1)	
	Current (%)	24 (63.2)	14 (36.8)	
HTN	Yes (%)	30 (40.0)	45 (60.0)	0.73 (0.26)
	No (%)	60 (32.6)	124 (67.4)	
CAD	Yes (%)	45 (56.3)	35 (43.7)	**0.26 (<0.001)**
	No (%)	45 (25.1)	134 (74.9)	
DM	Yes (%)	42 (31.6)	91 (68.4)	1.33 (0.27)
	No (%)	48 (38.1)	78 (61.9)	
NAFLD	Yes (%)	11 (28.2)	28 (71.8)	1.43 (0.35)
	No (%)	79 (35.9)	141 (64.1)	
ICA	Non-obstructive (%)	38 (28.4)	96 (71.6)	**0.71 (<0.01)**
	Minor (%)	20 (34.5)	38 (65.5)	
	Moderate (%)	14 (42.4)	19 (57.6)	
	Severe (%)	18 (52.9)	16 (47.1)	
PCI	Yes (%)	2 (15.4)	11 (84.6)	3.06 (0.13)
	No (%)	88 (35.8)	158 (64.2)	

Abbreviations: HTN, hypertension; DM, diabetes mellitus; NAFLD, non-alcoholic fatty liver disease; CAD, coronary artery disease; LT, liver transplantation; PCI, percutaneous coronary intervention.

mortality among patients with CAD detected on ICA. Among the 102 patients undergoing ICA with five-year survival data, diabetes mellitus was associated with reduced survival (OR 3.78; $p < 0.05$, Table 6). Numbers were too small to warrant analysis of post-transplant mortality in patients who underwent PCI.

4. Discussion

In this study we have identified a significant burden of CAD in LT candidates undergoing a clinically driven ICA. We have also demonstrated how ICA can be used in conjunction with non-invasive cardiopulmonary tools to decide on LT candidacy, and described comparable post-LT outcomes in selected patients with CAD identified pre-LT. The findings of this study are in keeping with previous reports, however, in addition we outline how ICA is used in patients declined for LT and report longer-term outcome data to 5 years post-LT for patients with CAD confirmed on ICA.

From our subgroup of 259 patients who underwent ICA during LT assessment, CAD was identified in 48% and moderate or severe CAD was present in 26%. This is similar to the reported CAD in 37% and obstructive CAD in 19% among LT candidates where a protocolised approach to ICA was adopted [8]. Other cohorts report data from patients who subsequently underwent LT, and found 24–26% with moderate/severe or obstructive CAD using a non-protocolised approach [11,13], and 10–33% with obstructive CAD from a protocolised approach [3,14]. Direct comparison between populations is not possible, in part due to the variable definitions of CAD on ICA. However, it is clear that there is a significant burden of CAD in LT candidates where ICA is performed, either due to clinical concerns or based on a protocol driven algorithm.

Table 6
Multi-variable analysis of all cause five-year mortality among patients with coronary artery disease.

Variables		OR	CI (95%)	p value
Age		0.95	0.88–1.03	0.19
Gender		1.22	0.29–5.17	0.79
Smoking	Ex-smoker	1.57	0.50–4.95	0.45
	Smoker	0.90	0.14–5.83	0.92
HTN		0.36	0.07–1.87	0.23
DM		3.80	1.17–12.29	**< 0.05**
CAD (on ICA)		2.26	0.72–7.05	0.16

Abbreviations: HTN, hypertension; DM, diabetes mellitus; CAD, coronary artery disease; ICA, invasive coronary angiography.

Within our cohort, old age, current smokers and previous history of CAD were all predictors of identifying CAD at ICA. This is consistent with well recognised risk factors for CAD in patients being considered for LT [4]. Various studies have documented different levels of association between traditional risk factors and CAD in patients with liver disease, which depends on the population being assessed. It is not the relative weight of any single risk factors that is used to confer risk to a good degree of accuracy [15]. This method has been used to recommend screening for CAD by many international societies [5]. However, due to the burden of 'silent' CAD in patients with liver disease and potential for revascularisation therapy, a more aggressive protocol using ICA may be more appropriate in patients with a combination of typical risk factors [3]. We would need to consider the cost effectiveness of this approach, especially with an increasingly multimorbid and elderly population being considered for transplant.

Guidelines for LT assessment recommend incorporating a non-invasive test for cardiac ischaemia [1,2], with positive findings on dobutamine stress echocardiography and myocardial perfusion scintigraphy associated with major adverse cardiac events and all-cause mortality post-LT [16]. Although there are significant limitations to their efficacy as a screening tool in patients with liver disease [3], particularly as patients may not achieve the required resting heart rate on dobutamine stress echocardiography due to peripheral vasodilatation or therapeutic use of beta blockers [17]. Furthermore on pooled analysis, despite having good specificity (82 and 74%), dobutamine stress echocardiography and myocardial perfusion scintigraphy did not have adequate sensitivity (28 and 61%) to rule out CAD [18]. At our centre we therefore do not routinely perform non-invasive stress testing and instead use CPET as a functional assessment, in conjunction with ICA in selected cases. A low AT on CPET is predictive of post-operative cardiovascular events and mortality following major abdominal surgery [19] and is a sensitive and specific predictor of early survival post LT [20].

In our practice, 52 patients with CAD on ICA demonstrated a satisfactory performance on CPET with 37 (71.2%) listed for LT, whilst some patients with existing clinical concerns (i.e. multiple risk factors) and a low anaerobic threshold on CPET could be declined for LT without ICA, thereby avoiding the potential procedural complications (Fig. 1). We find the presence of diabetes and older age were predictive of poor performance on CPET, which is likely to reflect poor

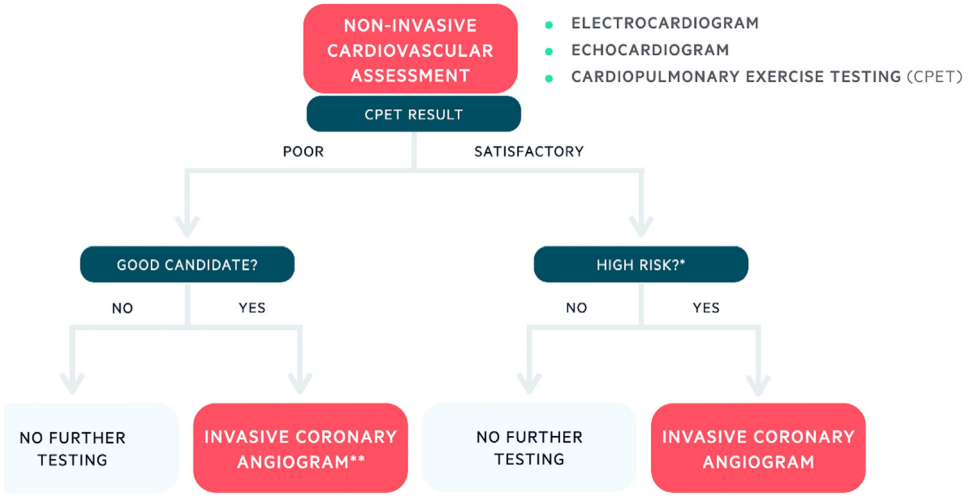

Fig. 1. Proposed flow-chart for the cardiovascular assessment of patients undergoing liver transplant assessment. * high risk usually defined as 3 or more cardiovascular risk factors or previous history of ischaemic heart disease (at the discretion of the transplant committee) ** consider repeat CPET whilst on the liver transplant waiting list.
Abbreviations: CPET, cardiopulmonary exercise test; ICA, invasive cardiac angiography.

cardiovascular fitness. However, there can be limitations to CPET results in deconditioned patients and technical challenges in sick patients with decompensated chronic liver disease [17], so the AT needs to be interpreted in the clinical context at time of testing. AT on CPET is a dynamic measure which can improve with reconditioning [17], it may be that CPET can be used to monitor high risk patients and their objective response to prehabilitation prior to LT [21] or cardiovascular fitness after coronary revascularisation. We have demonstrated how CPET can be used as an adjunct to the cardiac assessment, to both support the candidacy of patients with CAD on ICA, and help decline high risk patients without need for invasive testing.

Our all-cause five-year post-LT mortality in patients with CAD at ICA were comparable to patients without CAD. Existing data in the literature on post-LT outcomes in patients with CAD is conflicting; whilst presence of CAD has not been found to predict survival in some studies [10–12], meta-analysis including 5 studies identified an estimated all-cause mortality relative risk of 1.53 (95% CI, 1.00 −2.35) [16]. Furthermore, the effect of severity of CAD is not clear. Increasing severity of obstruction has been shown to be comparable to no CAD [11,12], however there was a trend towards worsening outcomes post-LT in patients with more severe CAD (P = .08), which may not have been appreciated due to small sample sizes in the cohort [3]. Our incomplete understanding may also stem from inconsistent definitions of positive ICA [16] and cardiovascular outcomes, which is reflected in the wide range of incidence rates of post-LT cardiovascular events [22]. On subgroup analysis of our patients with CAD who underwent LT, the presence of diabetes was associated with inferior all-cause five-year post-LT survival, which highlights a specific group who may need closer evaluation during transplant assessment.

PCI for coronary artery revascularisation was performed in 13 patients identified with CAD on ICA, with 11 subsequently listed for LT. There is an increasing body of evidence which supports non-inferior outcomes in patients who are adequately revascularised prior to LT [3,9,12,14]. Cardiovascular events post-LT, particularly in the early post-operative period, do occur in patients who have undergone PCI and may reflect a more susceptible myocardium despite revascularisation [12]. No safety signal from coronary stents and anti-platelet therapy has been reported in candidates awaiting LT, however the risk of variceal haemorrhage needs to be closely evaluated prior to embarking on anti-platelet therapy [23]. In a small cohort the presence of more diffuse multi-vessel CAD compared to no CAD was predictive of mortality [10]. Therefore, presence of diffuse non-prognostic multi-vessel CAD could represent the biggest factor in deciding transplant suitability, which reflects the small number of patients (7/23) with severe CAD who did not undergo PCI that were listed for LT in our population.

There are some important limitations to our study due to the retrospective analysis and single centre design. ICA was performed based on clinical concern and was not protocolised. A significant number of patients did not undergo CPET limiting our ability to draw conclusions on its role in transplant assessment. This was due to deconditioning or frailty. There is missing data on long-term outcomes with a proportion of patients transferred just for the peri-transplant period from other national and international centres. Further, there is no follow-up data on the long-term outcomes on patients who were declined for LT or on cardiovascular events. Data on one and three year mortality was not included because of a small proportion of outcomes. Finally, this was observational data collected over a defined time period and was not powered to detect outcome differences between subgroups.

The identification and treatment of CAD prior to LT is just one facet of the long-term management of these patients. Cardiovascular disease is a leading cause of non-hepatic morbidity and mortality post-LT [24], and cardiovascular risk factors can be accelerated by post-LT immunosuppression [25]. Although we have demonstrated a comparable five-year post-LT survival in our cohort with CAD it is important we maximise their longer term survival with aggressive management of cardiovascular risk factors post-LT. Lifestyle modifications are crucial to address the weight gain commonly seen post-LT [26], which also aids management of diabetes, hypertension and dyslipidaemia. Where weight loss is not achieved bariatric surgery can be considered [25], although there is limited data on safety and efficacy of this post-LT [27]. A beneficial effect of statins has been demonstrated on post-LT survival in patients with CAD and dyslipidaemia, and should be considered in at-risk patients [28]. It is clear that in parallel to this, institutions need to have clear pathways in place to educate patients on the long-term risks and enable other clinicians to have the confidence in treating cardiovascular risk factors in this multimorbid population [29].

5. Conclusions

In conclusion, data from our institution demonstrates how ICA can be used as a screening tool for CAD alongside non-invasive

cardiovascular assessments to determine candidacy for LT. Individuals with cardiovascular risk factors require an aggressive work-up for CAD, and ICA should be considered if non-invasive tools are not prohibitive for proceeding with LT. In selected patients with CAD, including those who underwent re-vascularisation, LT can be safely undertaken after multi-disciplinary assessment. This is of particular importance with the changing demographics of an older and multimorbid recipient population. Whilst their longer-term outcome after years on immunosuppressive medications has not been determined, patients with CAD can have comparable medium-term survival after LT.

CRediT authorship contribution statement

JSN, JR, MAH: conception and design of the study.

All authors: generation, collection, assembly, analysis and/or interpretation of data.

JSN, BN, SB, MAH: drafting or revision of the manuscript.

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Writing assistance

No writing assistance was provided.

Data availability

Datasets generated during and/or analysed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

No relevant conflicts of interest

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.liver.2022.100100.

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