

Adult liver transplantation in Johannesburg, South Africa (2004 - 2016): Balancing good outcomes, constrained resources and limited donors

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Background. Liver transplantation is the standard of care for the treatment of liver failure worldwide, yet millions of people living in sub-Saharan Africa remain without access to these services. South Africa (SA) has two liver transplant centres, one in Cape Town and the other in Johannesburg, where Wits Donald Gordon Medical Centre (WDGMC) started an adult liver transplant programme in 2004.

Objectives. To describe the outcomes of the adult liver transplant programme at WDGMC.

Methods. This was a retrospective review of all adult orthotopic liver transplants performed at WDGMC from 16 August 2004 to 30 June 2016 with a minimum follow-up of 6 months. The primary outcome was recipient and graft survival and the effect of covariates on survival. Kaplan-Meier survival analysis included all adults who underwent their first transplant for end-stage liver disease (ESLD) ($N=275$). Proportional hazards regression analysis using hazard ratios (HRs) was conducted to determine which covariates were associated with a significantly increased risk of mortality.

Results. A total of 297 deceased-donor liver transplants were performed during the study period; 19/297 (6.4%) were for acute liver failure (ALF) and the remainder were for ESLD. The median age of recipients was 51 years (interquartile range 41 - 59), and two-thirds were male. The most common cause of ESLD was primary sclerosing cholangitis. The median follow-up was 3.2 years, and recipient survival was characterised in the following intervals: 90 days = 87.6% (95% confidence interval (CI) 83.1 - 91.0), 1 year = 81.7% (95% CI 76.6 - 85.8), and 5 years = 71.0% (95% CI 64.5 - 76.5). Allograft survival was similar: 90 days = 85.8% (95% CI 81.1 - 89.4), 1 year = 81.0% (95% CI 75.8 - 85.2), and 5 years = 69.1% (95% CI 62.6 - 74.7). The most significant covariates that impacted on mortality were postoperative biliary leaks (HR 2.0 (95% CI 1.05 - 3.80)), recipient age >60 years at time of transplant (HR 2.06 (95% CI 1.06 - 3.99)), theatre time >8 hours (HR 3.13 (95% CI 1.79 - 5.48)), and hepatic artery thrombosis (HR 5.58 (95% CI 3.09 - 10.08)). The most common infectious cause of death was invasive fungal infection.

Conclusions. This study demonstrates that outcomes of the adult orthotopic liver transplant programme at WDGMC are comparable with international transplant centres. Management of biliary complications, early hepatic artery thrombosis and post-transplant infections needs to be improved. Access to liver transplantation services is still extremely limited, but can be improved by addressing the national shortage of deceased donors and establishing a national regulatory body for solid-organ transplantation in SA.

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There are only two adult liver transplant programmes in sub-Saharan Africa, and both are in South Africa (SA). The absence of these services for a billion people in this region contrasts starkly with widespread access in high-income countries. In SA, the first programme was established in 1988 at Groote Schuur Hospital in Cape Town and the second programme in 2004 at Wits Donald Gordon Medical Centre (WDGMC) in Johannesburg.^[1] WDGMC is uniquely situated as a private academic teaching hospital in the Faculty of Health Sciences at the University of the Witwatersrand. The hospital focuses on teaching

and training of specialists and sub-specialists and the provision of specialist care, including liver transplantation. Access to the liver transplant programme is based on need and all adults are prioritised for transplantation based on the severity of their illness. Referrals are widely received from state and private facilities.

Survival data on adult orthotopic liver transplants (OLTs) from international programmes have been published. Survival rates differ between middle-income and high-income countries because the volume of transplant procedures is usually much larger in

high-income countries. The Cape Town programme published a 10-year review (1988 - 1998) of 44 adult OLT procedures with 1- and 5-year patient survival rates of 72% and 61%, respectively.^[1] There are no data for adult liver transplants in SA after that time, despite major changes in the care and available treatment of transplant patients.

Objectives

To critically review the outcomes, constraints and challenges that persist for the adult liver transplant programme at WDGMC.

Methods

A retrospective record review was conducted of all adult (≥ 18 years) deceased-donor OLTs performed from the first transplant on 16 August 2004 to 30 June 2016, with a minimum follow-up of 6 months (31 December 2016). Approval for the study was obtained from the Medical Human Research Ethics Committee at the University of the Witwatersrand (ref. no. M140840). Data were extracted and cross-referenced using multiple sources: patient files, regulatory registers, organ procurement records, pathology laboratory and radiology services, surgical operation reports and ward admission records. Vascular and biliary complications were only included if they were confirmed radiologically and required an intervention (radiological and/or surgical). Postoperative biliary and vascular complications were independently reviewed by a radiologist. For all mortalities, cause of death was ascertained from clinical records, registers and postmortem reports, where available.

The following transplant recipient data were collected: age (on day of transplant procedure); gender; population group (black, mixed race, Asian/Indian and white); height; weight; body mass index (BMI, kg/m^2); cause of liver failure; time on wait list prior to transplantation (days); model for end-stage liver disease (MELD) score^[2] at time of transplant; ABO blood group; health status at time of transplant: inpatient/outpatient, diabetes mellitus, vascular disease, ascites; date of transplant; first or repeat transplant; allograft/s received (whole/split liver); operation time; cold ischaemic time; postoperative surgical morbidity: re-exploration by laparotomy, biliary and vascular complications, primary non-function of allograft; biopsy-proven acute rejection (within the first 90 days); and recipient and allograft survival.

The following deceased-donor data were collected: age (on day of donation); gender;

population group (as above); height; weight; BMI; ABO blood group; referral centre; length of hospital stay prior to donation; operation time for organ harvest; and cause of death. Donor data were used to calculate the donor risk index (DRI).^[3] All donors were heart-beating and brainstem dead; there was no donation after cardiac death.

Study data were collected and managed using Research Electronic Data Capture (REDCap), which is a secure, web-based application designed to support data capture for research studies hosted at the Faculty of Health Sciences, University of the Witwatersrand.^[4]

Statistical analysis

The DRI was calculated according to the formula provided by Feng *et al.*^[3] Percentage missing data have been included in all results in accordance with the Strobe guidelines for observational data.^[5] The association between primary sclerosing cholangitis and comorbid diseases was assessed using Fisher's exact test. Overall survival estimates were determined by the Kaplan-Meier method and there was no adjustment of the survival analyses for any variables. To determine whether there was an improvement in recipient survival over time, based on the premise that the unit would have undergone an initial learning curve, the survival analysis was divided into two eras. To ensure approximately equal numbers of transplants in each group, era 1 was from 16 August 2004 to 30 June 2012 and included 151 cases. Era 2 comprised all transplants performed from 1 July 2012 to 30 June 2016 and included 146 cases. The effect of covariates on unadjusted recipient survival for first transplants in patients with non-acute liver failure (ALF) was determined by Cox proportional hazards regression and included recipient age and BMI at transplant, recipient gender, DRI, allograft type, recipi-

ent length of hospital stay, operation time, cold ischaemic time, MELD score pre-transplant, health status pre-surgery (diabetes mellitus, ascites), centre experience (era 1 v. era 2), postoperative biliary and vascular complications, and cause of chronic liver disease (alcoholic and non-alcoholic steatohepatitis, autoimmune hepatitis, malignancy, primary sclerosing cholangitis, hepatitis B or C). The continuous variables were categorised for this analysis. Data were analysed using SAS version 9.4 (SAS Institute, USA). The 5% significance level was used.

Results

Between 16 August 2004 and 30 June 2016, there were 297 adult OLTs performed at WDGMC. Since inception of the programme, there has been a steady growth in the number of transplants performed per year (Fig. 1). While most recipient referrals were from the private sector, the relative proportions from the state sector almost doubled in era 2 (16/146, 11.0%) compared with era 1 (9/151, 6.0%). The majority of the procedures performed were liver-only transplants (293/297, 98.7%), and of these 16/293 (5.5%) were split grafts. There were 3 combined liver-kidney (1.0%), 1 combined liver-heart (0.3%) and 12 repeat transplants (4.0%).

Characteristics of all recipients at the time of the transplant are summarised in Table 1. Overall, the median age of recipients was 51 years, almost two-thirds were male, and the median MELD score was 17 (interquartile range (IQR) 13 - 22). Nine percent of recipients had a MELD score >30 . The indications for the transplant were ALF in 6.4% of cases (19/297) and end-stage liver disease (ESLD) in the remainder. Of the 6 patients who presented with drug-induced liver failure in the ALF group, 3 were HIV-positive with efavirenz-induced hepatotoxicity.

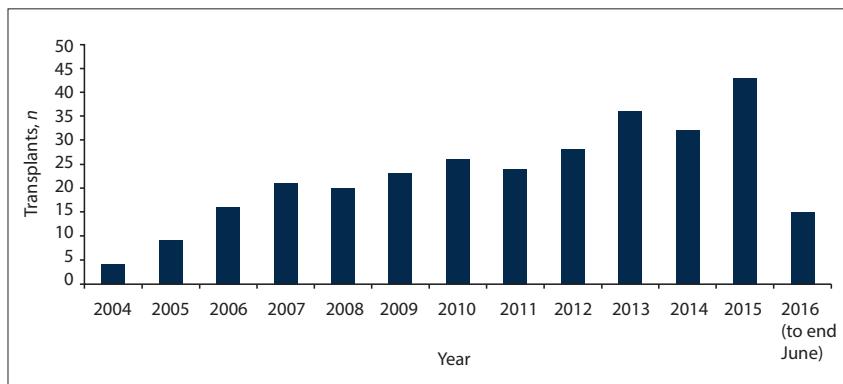


Fig. 1. Adult orthotopic liver transplants performed per annum at Wits Donald Gordon Medical Centre from 16 August 2004 to 30 June 2016.

Table 1. Characteristics of adult OLT recipients at the time of transplant

| Variable | Overall (N=297) |
|---|---------------------|
| Referral site, n (%) | |
| State | 25 (8.4) |
| Private | 272 (91.6) |
| Age (years), median (IQR) | 51 (41 - 59) |
| Gender, n (%) | |
| Male | 173 (58.2) |
| Female | 124 (41.8) |
| Population group, n (%) | |
| White | 204 (68.7) |
| Black | 53 (17.8) |
| Indian/Asian | 28 (9.5) |
| Mixed | 8 (2.7) |
| Missing | 4 (1.3) |
| Blood group, n (%) | |
| O | 138 (46.5) |
| A | 112 (37.7) |
| B | 33 (11.1) |
| AB | 12 (4.0) |
| Missing | 2 (0.7) |
| BMI (kg/m^2), median (IQR) (N=292, 98.3%) | 26 (23 - 31) |
| Disease severity, n (%) | |
| Ascites, present/missing | 193 (65.0)/5 (1.7) |
| Diabetes mellitus (type 2 only, no type 1), present/missing | 56 (18.9)/4 (1.3) |
| Vascular disease (cerebral, cardiac, peripheral), present/missing | 32 (10.8)/24 (8.1) |
| Hospitalisation, yes/missing | 52 (17.5)/43 (14.5) |
| Dialysis, yes/missing | 12(4.0)/4 (1.3) |
| MELD score, median (IQR) | 17 (13 - 22) |
| MELD score, n (%) | |
| <10 | 31 (10.4) |
| 10 - 20 | 168 (56.6) |
| 21 - 30 | 68 (22.9) |
| >30 | 27 (9.1) |
| Missing | 3 (1.0) |
| Cause of ALF, n (%) (N=19, 6.4%) | |
| Primary non-function of allograft | 8 (2.7) |
| Drug-induced | 6 (2.0) |
| Infection | 4 (1.4) |
| Acute Wilson's disease | 1 (0.3) |
| Cause of ESLD, n (%) (N=278, 93.6%)* | |
| Cholestatic (biliary) cirrhosis | |
| Primary sclerosing cholangitis | 74 (24.9) |
| Primary biliary cirrhosis | 20 (6.7) |
| Vanishing bile duct syndrome | 6 (2.0) |
| Missing | 1 (0.3) |
| Non-cholestatic cirrhosis | |
| Non-alcoholic steatohepatitis | 58 (19.5) |
| Alcoholic steatohepatitis | 53 (17.8) |
| Autoimmune hepatitis | 34 (11.4) |
| Hepatitis C | 15 (5.1) |
| Hepatitis B | 12 (4.0) |
| Cryptogenic | 12 (4.0) |
| Other† | 6 (2.0) |
| Malignancy | |
| Hepatocellular carcinoma | 23 (7.7) |
| Hepatic epithelioid haemangioendothelioma | 2 (0.7) |

Continued ...

Table 1. (continued) Characteristics of adult OLT recipients at the time of transplant

| Variable | Overall (N=297) |
|--|-----------------|
| Hepatic embryonal sarcoma | 1 (0.3) |
| Metastatic liver disease (colorectal cancer) | 1 (0.3) |
| Cholangiocarcinoma | 3 (1.0) |
| Ductal carcinoma (other than cholangiocarcinoma) | 1 (0.3) |
| Missing | 1 (0.3) |
| Venous outflow obstruction | |
| Budd-Chiari syndrome | 16 (5.4) |
| Metabolic | |
| Alpha-1-antitrypsin deficiency | 5 (1.7) |
| Haemochromatosis | 4 (1.3) |
| Wilson's disease | 2 (0.7) |
| Oxalosis | 2 (0.7) |
| Erythropoietic porphyria | 1 (0.3) |
| PFIC (type 2 – biopsy proven) | 1 (0.3) |

OLT = orthotopic liver transplant; BMI = body mass index; IQR = interquartile range; MELD = model for end-stage liver disease; ALF = acute liver failure; ESLD = end-stage liver disease; PFIC = progressive familial intrahepatic cholestasis.
*Values add up to more than 100% owing to multiple comorbidities.
[†]Autosomal dominant polycystic kidney disease n=3, sarcoidosis n=1, drug-induced n=1, infectious cause suspected but not identified n=1.

In the group with ESLD, the median time on the wait list was 54 days (IQR 23 - 130). As expected, primary sclerosing cholangitis was the most common aetiology (74/297, 24.9%), followed by almost equal numbers of alcoholic (53/297, 17.8%) and non-alcoholic steatohepatitis (58/297, 19.5%). Patients with primary sclerosing cholangitis had a significantly higher prevalence of ulcerative colitis (26.4%; $p<0.0001$) and Crohn's disease (9.7%; $p<0.0001$) compared with those who did not have primary sclerosing cholangitis, for whom the prevalences of ulcerative colitis and Crohn's disease were 1.4% and 0.5%, respectively. Malignancies, most commonly hepatocellular carcinoma, comprised 10.8% (32/297), with a similar proportion of chronic hepatotropic viral infections (9.4%, 28/297), of which hepatitis C was most frequent.

The deceased-donor pool comprised mostly young white males who died from trauma. This was reflected in the relatively low median DRI of 1.61 (IQR 1.37 - 1.90) (Table 2).

Postoperative surgical complications are detailed in Table 3. Primary non-function of the allograft occurred in 8 cases (2.7%). Approximately 20% of patients required an exploratory laparotomy post-procedure. Overall, the most frequent complications were of biliary origin (62/297, 20.9%). The biliary leak rate was 9.1% (27/297) and most leaks occurred within the first 90 days after transplant. Conversely, the biliary stricture rate was 13.1% (39/297) and most occurred after 90 days. By far the most common vascular complication was hepatic artery thrombosis (HAT), with an incidence rate of 3.7% (11/297) in the first 30 days post-transplant.

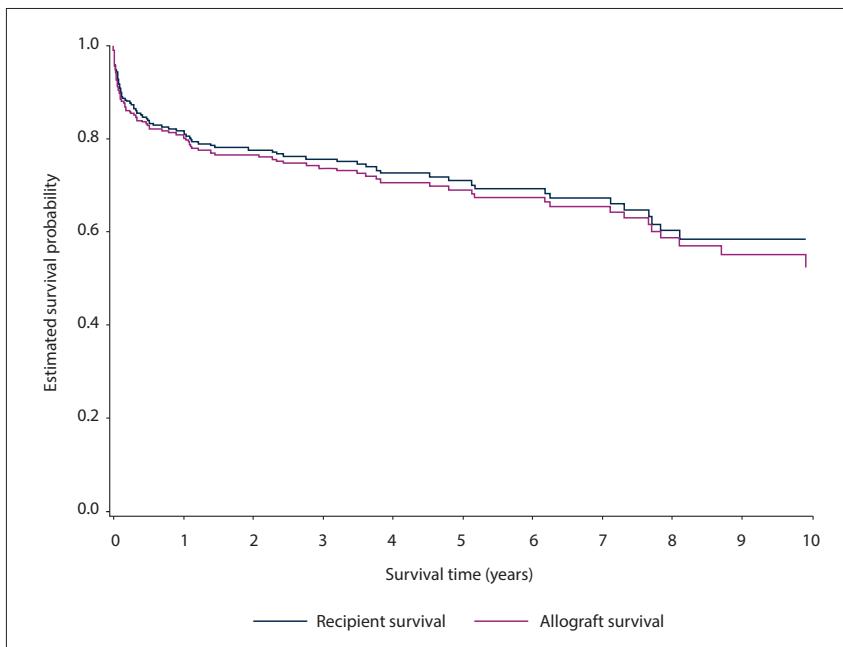


Fig. 2. Unadjusted adult orthotopic liver transplant survival for allograft and recipient at Wits Donald Gordon Medical Centre (first transplant only, non-acute liver failure aetiology, N=275)

Median follow-up was 3.2 years. Using the Kaplan-Meier method, recipient survival for first transplants for end-stage liver disease ($n=275$) was estimated at the following intervals: 90 days = 87.6% (95% confidence interval (CI) 83.1 - 91.0), 1 year = 81.7% (95% CI 76.6 - 85.8), and 5 years = 71.0% (95% CI 64.5 - 76.5). Allograft survival was similar: 90 days = 85.8% (95% CI 81.1 - 89.4), 1 year = 81.0% (95% CI 75.8 - 85.2), and 5 years = 69.1% (95% CI 62.6 - 74.7) (Fig. 2). While there was improved recipient survival in era 2 compared with era 1, this was not statistically significant ($p=0.095$) (Fig. 3).

Using proportional hazards regression analysis, the following covariates were

associated with a significantly increased risk of mortality: recipient age >60 years at time of transplant (compared with age 18 - 39 years) (hazard ratio (HR) 2.06 (95% CI 1.06 - 3.99)); theatre time >8 hours (compared with 6 - 8 hours) (HR 3.13 (95% CI 1.79 - 5.48)); postoperative biliary leaks (HR 2.0 (95% CI 1.05 - 3.80)); any vascular complication (HR 3.78 (95% CI 2.30 - 6.22)); and HAT (HR 5.58 (95% CI 3.09 - 10.08)). There was no significant association with any aetiology of chronic ESLD and postoperative mortality (appendices 1 and 2, available from the corresponding author on request: june.fabian@mweb.co.za). There was a substantial mortality risk associated

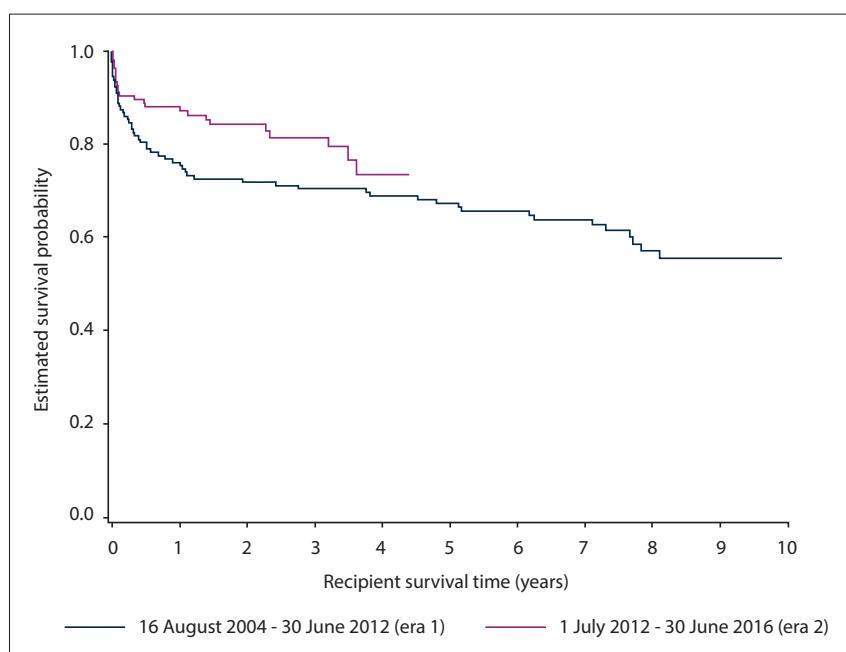


Fig. 3. Adult liver transplant recipient and allograft survival at Wits Donald Gordon Medical Centre (first transplant only, non-acute liver failure, N=275). Recipient survival: era 1: 90 days = 85.2% (95% CI 78.2 - 90.0) and 1 year = 76.1% (95% CI 68.1 - 82.2); era 2: 90 days = 90.2% (95% CI 83.8 - 94.2) and 1 year = 87.9% (95% CI 81.0 - 92.4). (CI = confidence interval.)

with 'redo' or second transplants (HR 4.6 (95% CI 2.3 - 9.3)).

Postmortem reports were available for almost half of the recipients who died in the first 90 days (20/47). Infectious aetiologies were the most common primary cause of death (9/20), and a significant contributing factor in 4 additional cases. Allograft failure (5/20), pulmonary thromboembolic disease (2/20), myocardial ischaemia (2/20) and cerebrovascular accident (1/20) comprised the remaining primary causes of death (1 case was undetermined). When infection was cited as the primary cause of death, the lungs (*n*=4) and gut (*n*=4) were the most common sources. Fungi were the organisms most commonly identified post mortem, namely *Candida* (*n*=2), aspergillosis (*n*=4), blastomycosis (*n*=1) and mucormycosis (*n*=1). It could not be established whether these organisms were identified antemortem.

Discussion

In the adult OLT programme at WDGMC, patient and graft survival are comparable to local and international transplant centres. The Cape Town programme published a 10-year review (1988 - 1998) of 44 adult OLT procedures with 1- and 5-year patient survival rates of 72% and 61%, respectively.^[1] The improved survival observed in our programme, 81.7% at 1 year and 70.0% at 5 years, is a more contemporary experience and may reflect a combination of advances in immunosuppressive therapy such as the

advent of tacrolimus, and improvements in surgical experience with a relatively higher transplant volume. More recently, other middle-income countries such as Thailand, India and Brazil have published similar outcomes.^[6-8] Collectively, it is difficult to compare the outcomes of middle-income countries with high-income regions such as Europe and the USA, as the transplant milieu is different and volumes are substantially smaller. However, while early survival rates (90 days and 1 year) do appear to be lower in middle-income countries, survival rates after 1 year are equivalent to high-income regions.^[9-11]

The most common indication for liver transplant in our study was primary sclerosing cholangitis, followed by non-alcoholic and alcoholic steatohepatitis. This was similar to the findings published from Cape Town, where the three most common indications for liver transplant were post-necrotic and alcoholic cirrhosis, and primary sclerosing cholangitis.^[1] In both SA sites, primary sclerosing cholangitis was the cause of ESLD in 22 - 25% of liver transplant recipients, compared with 5% in Europe and 9% in the USA.^[10-12] Cholestatic causes of liver failure are also less frequent indications for liver transplant in Asia, where hepatitis B infection is the predominant cause of ESLD.^[12] Internationally, post-transplant survival for patients with ESLD due to primary sclerosing cholangitis is usually better than for other causes, but this was

not demonstrated in our study (appendix 1, available from the corresponding author on request: june.fabian@mweb.co.za).^[10-12] One explanation may be that our sample size was relatively small. As an infectious cause of ESLD, hepatitis C (5.1%) was more common than hepatitis B (4.0%), which is unexpected in SA but may be explained by the predominance of white OLT recipients in this cohort.

The emergent cases of ALF secondary to fixed-dose combination antiretroviral therapy (ART) for treatment of HIV infection deserve mention. The spectrum of histopathological changes in patients presenting with drug-induced liver injury secondary to ART shows considerable variation. Biopsies in some patients show features of chronic hepatitis, including portal inflammation with or without lobular inflammation, and variable fibrosis, while in others the pathological injury is much more severe. Many patients recover with interruption of treatment, but in severe cases this complication can be catastrophic as access to liver transplantation is limited. The implications of ALF caused by fixed-dose combinations of ART are particularly relevant as SA has the largest HIV treatment programme in the world.

Biliary complications are an important cause of postoperative morbidity and mortality, and the international incidence varies from 5% to 25%.^[13,14] In our programme, the incidence of all biliary complications was relatively high (20.9%) (Table 1). Reported incidence rates for biliary leaks and strictures range from 5% to 10% and 9% to 12%, respectively.^[14] Our results were consistent with these findings for biliary leaks (9.1%) and strictures (13.1%) (Table 3).

HAT is a dreaded complication of liver transplantation, with most cases occurring in the early post-transplant period. There is no standard definition of early HAT (eHAT), ranging from within 2 weeks to 100 days after liver transplantation. In a systematic review that defined eHAT as occurring within the first 2 months of transplant, a worldwide decline in incidence rates over time has been demonstrated, dropping to 2.9% in adults in high-volume centres. Our eHAT rate of 3.7% was higher than the rates observed in high-volume centres but comparable to rates observed in other low-volume centres (5.8%).^[15]

Based on a limited autopsy series of deaths that occurred in the first 90 days, sepsis was unequivocally the most common primary cause of death, and the most frequent organisms identified post mortem

Table 2. Characteristics of deceased donors and the DRI

| Variable | Overall (N=297) |
|---|--------------------|
| Age (years), median (IQR) (N=291, 98.0%) | 34 (21 - 45) |
| Population group, n (%) | |
| White | 240 (80.8) |
| Black | 23 (7.75) |
| Mixed | 23 (7.75) |
| Indian/Asian | 8 (2.7) |
| Missing | 3 (1.0) |
| Gender, n (%) | |
| Male | 179 (60.3) |
| Female | 118 (39.7) |
| BMI (kg/m ²), median (IQR) (N=273, 91.9%) | 25.5 (4.5) |
| Blood group | |
| O | 170 (57.2) |
| A | 100 (33.7) |
| B | 24 (8.1) |
| AB | 3 (1.0) |
| Cause of death | |
| Trauma | 158 (53.2) |
| CVA | 109 (36.7) |
| Anoxia | 9 (3.0) |
| Other | 19 (6.4) |
| Missing | 2 (0.7) |
| Allocation of deceased-donor organ | |
| Regional | 193 (65.0) |
| National | 104 (35.0) |
| DRI, n (%) | |
| ≤1.00 | 1 (0.3) |
| 1.01 - 1.20 | 23 (7.7) |
| 1.21 - 1.40 | 51 (17.2) |
| 1.41 - 1.60 | 48 (16.2) |
| 1.61 - 1.80 | 49 (16.5) |
| 1.81 - 2.00 | 38 (12.8) |
| >2.00 | 48 (16.2) |
| Missing | 39 (13.1) |
| DRI, median (IQR) | 1.61 (1.37 - 1.90) |

DRI = donor risk index; IQR = interquartile range; BMI = body mass index; CVA = cerebrovascular accident.

were fungi. This has been described previously and raises some pertinent considerations for clinical practice such as whether certain high-risk individuals should receive antifungal prophylaxis, for example those undergoing 'redo' transplants or with a pretransplant MELD score of ≥20.^[16] There are also diagnostic challenges because fungal infections may be missed without a tissue sample, such as a lung or liver biopsy specimen.^[17] We currently have a high index of suspicion for fungal infection in our programme and use trends in beta-D glucan and galactomannan levels to initiate broad-spectrum antifungal therapy. Where possible, an attempt is made to obtain biopsy material to confirm the diagnosis of invasive fungal infection.

Despite favourable outcomes, the adult OLT programme at WDGMG faces numerous challenges. For countries north of our borders, there is no access to liver transplantation and this is unlikely to change in the immediate future. Both the SA transplant programmes are located in large urban cities, making access difficult for those who live in semi-urban and rural areas. Further restrictions to access are imposed by a two-tiered healthcare system that favours the private sector and a national paucity of organ donors. Although

the liver transplant centre in Cape Town is located in the state sector, the volume of transplants performed annually is relatively low. Without active, high-volume participation by state hospitals in solid-organ transplantation, access to these services will remain limited. The hybrid programme at WDGMG makes provision for access to liver transplantation based on need, regardless of 'payer' status. This reflects an evolution of policy, based on the recognition that expansion of transplant services in the state sector has been slow and liver transplantation is a low-demand but resource- and cost-intensive healthcare service. The increasing number of state patients seen in era 2 reflects this change and is welcomed.

The number of transplants performed annually at WDGMG is not limited by capacity or resources, but rather by a dearth of donors. This highlights one of the greatest barriers to increasing solid-organ transplant volumes in SA and can only be addressed if a multifaceted approach is fully endorsed by national government for: (i) widespread public engagement and education about organ donation; (ii) the establishment of active organ procurement programmes in all hospitals; (iii) developing more transplant centres; and (iv) expanding the deceased and living organ donor pool.

Table 3. Postoperative complications in adult OLT transplant recipients

| Complication | Overall (N=297) |
|---|--|
| Primary non-function of allograft, n (%) | |
| Yes | 8 (2.7) |
| No | 289 (97.3) |
| Re-exploration (via laparotomy), n (%) | |
| Yes | 56 (18.8) |
| No | 239 (80.5) |
| Missing | 2 (0.7) |
| Vascular complication, n (%) | |
| Yes | 39 (13.1) |
| No | 257 (86.6) |
| Missing | 1 (0.3) |
| Type of vascular complication (N=39, 13.1%), n (%)* | |
| Portal vein thrombosis | 11 (28.2) 5 early (\leq 30 days), 6 late ($>$ 30 days) |
| Portal vein stenosis | 2 (5.1) 0 early, 2 late |
| Inferior vena cava thrombosis | 3 (7.7) 2 early, 1 late |
| Inferior vena cava stenosis | 3 (7.7) 0 early, 3 late |
| Hepatic artery thrombosis | 19 (48.7) 11 early, 8 late |
| Hepatic artery stenosis | 3 (7.7) 1 early, 2 late |
| Hepatic artery pseudoaneurysm | 2 (5.1) 1 early, 1 late |
| Hepatic artery rupture | 1 (2.6) |
| Biliary complication, n (%) | |
| Yes | 62 (20.9) |
| No | 235 (79.1) |
| Type of biliary complication (N=62, 20.9%), n (%)* | |
| Biliary leak | 27 (43.6) 25 early (\leq 90 days), 2 late ($>$ 90 days) |
| Biliary stricture | 39 (62.9) 12 early, 27 late |
| Acute biopsy-proven rejection of allograft, n (%) | |
| Yes | 22 (7.4) |
| No | 275 (92.6) |

OLT = orthotopic liver transplant.

*Values add up to more than 100% because some recipients had more than one complication.

Transplantation programmes require substantial resources, and prioritisation of these services within the national health agenda can be problematic, particularly in middle-income countries. The growth of such services may only be ethically justifiable if the outcomes achieved are comparable to an accepted standard. Auditing local practice as part of the governance process in each transplant unit, a national liver transplant registry, and establishing a national regulatory body for solid-organ transplantation would be appropriate first steps.

Study limitations

This study has some limitations. It was retrospective and there were missing data, particularly regarding post-transplant infection and early v. late causes of death. Most recipient referrals were from the private sector, so this sample cannot be regarded as representative of the SA population. However, this research has highlighted areas for improvement in our clinical practice, such as reducing biliary

and vascular complications and addressing antifungal prophylaxis in high-risk individuals. It also exposes persistent systemic inequities that compromise access to this form of care for most South Africans and demonstrates the complexities of providing liver transplantation services in a middle-income country, which is relatively well-resourced compared with other sub-Saharan African countries.

Conclusions

In this study, the outcomes of the adult liver transplant programme at WDGMC in Johannesburg were comparable with international centres. Primary sclerosing cholangitis was the most common cause of chronic ESLD, which concurs with similar findings from Cape Town, but differs from international findings in the East and the West. Risk factors associated with increased mortality were recipient age >60 years at the time of transplant, operation time >8 hours, development of postoperative biliary leaks and vascular complications, particularly hepatic artery thrombosis. The biliary

complication and eHAT rates were higher than those seen in high-volume centres and remain areas for improvement. Inequities in access to care and low donor rates remain significant challenges for liver transplantation in SA.

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