Contemporary Management of Median Arcuate Ligament in Liver Transplantation

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Background. Median arcuate ligament (MAL) can impair arterial inflow during orthotopic liver transplantation (OLT). Furthermore, approaches to ensure optimal vascular inflow in the presence of MAL is not standardized. Methods. We undertook a systematic review according to the Cochrane systematic review protocol and Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We analyzed the incidence of MAL, investigations, treatment options, and potential complications associated with MAL intervention in patients undergoing OLT. After the exclusion criteria were implemented, the dataset from the final 21 manuscripts yielded 117 patients who underwent a liver transplant in the presence of MAL. Results. The incidence of MAL in patients undergoing OLT is between 1.6% and 12%. In 63.2% of cases, an open approach for MAL intervention was undertaken. Hepatic artery thrombosis developed in 17% (7) patients without MAL intervention versus 2.6% (2) after MAL intervention. Seven grafts (5.9%) were lost after OLT in patients with MAL. Three (3.9%) patients developed arterial stenosis post-MAL intervention. Conclusions. We propose an algorithm for intraoperative assessment and management of liver transplant arterial inflow in the presence of MAL based on the hepatic artery flow changes with respiration, following clamping of the recipient gastroduodenal artery. In the presence of a 30%–50% flow variation on respiration, the arterial inflow should be established preserving additional inflow from the recipient gastroduodenal artery. Consider an open MAL release if the flow remains insufficient. A poor arterial flow with no variation with respiration and lack of evidence of aortoiliac atherosclerosis indicates the need for arterial jump graft.

INTRODUCTION

Adequate blood flow through the newly anastomosed hepatic artery (HA) is essential for the short and long-term outcome of the transplanted liver. The flow can be impaired for a variety of reasons, which could include the presence of a median arcuate ligament (MAL) at the origin of the celiac trunk.

The MAL is a fibrotendinous ligament connecting the roots of the left and right diaphragmatic crura, which, along with the ganglions and nerve plexus, can cause extrinsic compression of the celiac trunk.1-3 Although the incidence of MAL in the general population ranges from 12% to 55%,4,6 it appears to be much lower in patients undergoing liver transplantation ranging between 2% and 12%.4,11 Fukuzawa et al12 reported an incidence of MAL of up to 10%, although this estimation is based on the number of patients who required dissection of the ligament to restore good HA pulsation.

The presence of MAL combined with a high aortic origin of the celiac axis leads to a reduced flow through the celiac trunk and its’ tributaries.3 There are few reports in the literature describing the presence of MAL in the liver transplant population and, in particular, the optimal strategy to ensure adequate flow in the HA postperfusion in these situations. Jurim et al13 and Paulson et al14 have demonstrated that the presence of MAL is associated with a reduction in the mean HA velocity from 425 mL/min to 200 mL/min, especially during the expiratory phase of the respiratory cycle.13,14 As expiration comprises two-thirds of the cycle, the arterial blood flow in a liver could thus be compromised in the presence of MAL.10 This becomes critical in liver transplantation, in which collateral vessels do not contribute to the arterial flow, and potentially results in HA thrombosis (HAT), leading to ischemic cholangiopathy, cholangitis, and graft failure.13 The incidence of HAT in liver transplant recipients with MAL is reported at 20% compared with 6.9% in patients without MAL.4

The diagnosis of MAL on preoperative imaging is not always clear but may be suggested by stenosis at the origin of the celiac axis without the presence of vascular calcifications.
As a result, the presence of a MAL may only be suspected intraoperatively because of poor arterial flow. Furthermore, the optimal surgical approaches for ensuring an optimal vascular inflow in the presence of MAL are not standardized and have included the release of the MAL,13 HA reconstruction without the release of MAL,15 aortohepatic jump grafts,9 radiological stenting of celiac axis,16 and delayed laparoscopic MAL release approach.17

Therefore, we undertook a systematic review that explores the incidence of MAL, investigations, treatment options, and potential complications from various surgical approaches in patients undergoing liver transplantation. We propose an algorithm for intraoperative assessment and management of liver transplant arterial inflow in the presence of MAL.

MATERIALS AND METHODS

Study Design

This review, based on the Cochrane systematic review protocol,18 explores the incidence, investigation, and treatment options in patients undergoing liver transplantation with MAL.

The Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines were used for reporting.19

Inclusion Criteria

The inclusion criteria for the selection of manuscripts were all reports of patients with a MAL undergoing liver transplantation. No age limits were placed, to ensure the capture of all patients with MAL undergoing liver transplantation and their management options. Publications were restricted to the English language. Because there were no randomized controlled trials in the management of these groups of patients, multicenter reports, observations, single-center series, and case reports were included.

Exclusion Criteria

Reviews, letters to editors, book chapters, manuscripts with duplication of data, perspectives, animals, and manuscripts containing incomplete data were excluded.

Information Sources

A maximally sensitive search strategy was developed. The literature was searched systematically using Ovid MEDLINE, Excerpta Medica database (EMBASE), SCOPUS, Google Scholar, Web of Science, and the Cochrane library databases for publications, from the inception of databases to February 2, 2021. The MeSH Headings used were truncated to broaden the search in combination with a Boolean operator to ensure the capture of all topic-related manuscripts. The headings included were “median arcuate ligament,” “Dunbar syndrome,” “celiac artery compression,” “Harjola-Marable syndrome,” and “liver transplant.”

Study Selection

The bibliographic reference manager software EndNoteX9.3.3 (Clarivate, Philadelphia, PA) was used to search for references from databases. These references were assessed for eligibility from their titles and abstracts, and the selected manuscripts were screened against inclusion and exclusion criteria. The reference list of the selected manuscripts was searched and relevant manuscripts within the list were hand-picked.

When similar or follow-up results were reported, in different manuscripts, the article containing the complete and latest dataset was selected.

Quality Assessment

The quality of each study was assessed using a methodological quality assessment tool for case reports and case series as described by Murad et al.20 An overall assessment of the quality of the studies was performed, rather than an aggregate score because some of the questions in the assessment tool were felt to be more critical compared with others.20

Data Extraction and Analysis

The extracted data were categorized as follows: demographic profile, type of cirrhosis, preinterventional investigation, type of intervention, and outcome including graft loss and death.

These data were then populated onto a predefined Microsoft Excel database. Data were presented as median (range), and nonparametric tests were used for comparisons unless otherwise specified.

RESULTS

Systematic Review and Study Characteristics

The initial literature search was performed using the Ovid MEDLINE, Excerpta Medica database (EMBASE), SCOPUS, Google Scholar, Web of Science, and the Cochrane library databases for publications with the help of Boolean operators. This search yielded 199 manuscripts. After the exclusion criteria were implemented, the dataset from the final 21 manuscripts yielded 117 patients who underwent a liver transplant in the presence of MAL. The PRISMA flow diagram in Figure 1 represents the article selection process.

No randomized control trials were retrieved. The study quality of the selected manuscripts ranged from poor to good.

Demographics

The median age for the adult and pediatric patient populations was 51 y (range 21–67 y) and 14 y (range 1–17 y), respectively. The male to female ratio was 1:0.64 (adults) and 2:1 (pediatric patients).

Incidence and Classification of Severity of MAL

The reported incidence of a MAL in patients undergoing liver transplantation ranged between 1.6% and 12%.3,4,9,12,13,15

There was a lack of uniformity in the severity classification of MAL across the manuscripts,9,15 and the majority of the transplanted organs were from deceased donors.1,7–9,11,13,21–23

Presentation Postorthotopic Liver Transplant Requiring MAL Intervention

The most common postorthotopic liver transplant (OLT) presentations that necessitated a MAL intervention were right upper quadrant pain,21 worsening liver function tests,17,22–24 HA thrombosis,1,23,26 hematoma,1 and hypovolemic shock.7

Timing of Decision to Intervene

Based on available data, the decision to undertake a MAL intervention was taken before an OLT in 43%, intraoperatively in 43% and postoperatively in 14% of patients.1,4,6,8,11–13,16,17,21–25,27–29
Type of MAL Intervention

Seventy-four (63.2%) patients had an open approach for their MAL intervention compared with 2 (1.7%) patients who had a laparoscopic approach for their MAL intervention. One (0.85%) patient underwent a radiologically inserted stent of the suspected MAL and had reinsertion of another stent because of the collapse of the first stent.

Investigations

Radiological Investigations Before MAL Intervention

Computerized tomography (CT) and duplex ultrasound were the radiological modalities most frequently used to diagnose and facilitate the management of MAL.

Digital subtraction angiography (DSA) was used in 2 patients. Sun et al. used DSA in combination with CT scan and Duplex ultrasound before MAL intervention. In the second patient, DSA was used as part of the radiological intervention to place a stent across a MAL affected celiac axis.

MRI was not used to aid management in the selected studies.

Post-MAL Intervention Investigations

The majority of the manuscripts used postoperative ultrasound Doppler to assess the adequacy of the hepatic arterial flow after MAL intervention. Fifteen manuscripts note an improvement in the liver function tests, post-MAL intervention. The rest of the manuscripts did not have any available data.

Type of Transplant Arterial Inflow

Sixty patients had a donor HA anastomosis to recipient HA preserving the gastroduodenal artery (GDA) with open MAL intervention. Four patients had a donor HA to recipient celiac/splenic artery anastomosis with MAL intervention. Three patients had donor HA to recipient HA with MAL intervention. Fourteen patients had HA anastomosis, preserving GDA without MAL intervention. Two patients had HA to accessory vessel anastomosis for arterial inflow without MAL intervention (Table 1).

Splenic artery ligation, splenectomy, and splenic artery coil embolization were undertaken in 1 patient each to increase the flow through the hepatic arterial anastomosis.

Thirty patients had the arterial inflow established using an aortohepatic jump graft (AHJG). In 25 patients, AHJG was undertaken without a MAL intervention, whereas in 5 patients, the AHJG was created after a MAL interventional failure (Table 1).

One patient had radiological stenting of the celiac axis, after liver transplantation. A reinsertion of an oversized stent was required because the near-complete recoil of the initial stent felt to be due to MAL. Although moderate residual stenosis persisted after the second stent placement, a sustained improvement in the liver function tests and normalization of duplex ultrasound scanning parameters was noted.

Complications

Complications in Patients Without MAL Intervention During OLT

Seven patients (17%) developed HA thrombosis post-OLT without MAL intervention. One patient (2.4%) developed liver infarction and another developed a liver abscess. Residual moderate stenosis of the HA was noted in 1 patient (2.4%). A pediatric patient developed an asymptomatic rise in liver function tests. All of these patients had to have a subsequent MAL intervention or retransplant because of graft loss.
Complications Related to MAL Intervention

In the reports included in this review, 3 patients (3.9%) were noted to have developed arterial stenosis.15 Two patients (2.6%) had a celiac trunk injury during MAL intervention, which required a supra-renal aortic conduit. 13 Two patients (2.6%) developed arterial thrombosis after MAL intervention.

Overall Graft Loss and Mortality

Seven grafts (5.9%) were lost after OLT in patients with a MAL. Of the 7 grafts that were lost, 1 patient developed graft-related gall bladder cancer but died of an unrelated metastatic epidermoid tongue cancer.28 The remaining 6 patients had HA thrombosis.1,4,9,23,29 One of these had an early HAT after an aortohepatic jump graft and underwent a reoperation with prosthetic graft interposition. 4 Five (4.3%) of these patients did not have MAL release procedures before their OLT and underwent MAL-related surgery and a retransplant.1,4,9,23

One patient died of graft-related reasons, due to failure of poststenotic dilatation of the celiac axis. 15 Three nongraft-related complications resulted in the death of these patients post-liver transplant.9,28

DISCUSSION

In 1917, in his “Study of celiac axis artery,” Lipshutz described the phenomena of compression of the abdominal aorta.31 Almost 50 y later, Harjola and Dunbar described the MAL syndrome separately.32,33 It was not until 1972 that Colapinto et al demonstrated the presence of the MAL using CT.7

Imaging modalities including CT or MRI aid the diagnosis, especially a phase-contrast MRI.34 Given the changes in flow with the respiratory cycle, Sun et al3 have suggested an end-inspiratory arterial phase and an end-expiratory portovenous phase with sagittal arterial reconstruction in cases where a CT angiogram is used for diagnosis.

Acquiring CT or MRI images in end-inspiration helps with the diagnosis of MAL.5 Poststenotic dilatation and the presence of pancreaticoduodenal collaterals support the diagnosis of significant celiac artery stenosis.10 Additionally, assessing the direction of flow through the GDA helps estimate the extent of stenosis. A reversed flow through the GDA was noted in stenoses >50%, whereas variable flow patterns were noted even when the flow was between 34% and 60%.34 That said, the correlation between the GDA diameter and the degree of celiac artery stenosis is weak.34 Jurim et al suggested that flow variations during respiration may be a better diagnostic aid; published data seems to suggest a flow drop through the celiac artery with MAL to around 200 mL/min during expiration13 from a flow of over 400 mL/min after reperfusion.14 Although these figures are highly dependent on several factors, it is the large variation in flow measurements during respiratory phases that are more important rather than absolute figures.

Another finding that is highly suggestive of the presence of MAL is the “hooked” appearance of the celiac artery on sagittal plane reconstructions due to the narrowing of the proximal portion of the celiac artery.2

There are several reasons that may cause a decreased flow through the HA during a liver transplant. A decrease in flow due to atherosclerosis can be differentiated from MAL by the absence of variation with respiration, especially when there is evidence of aortoiliac atherosclerotic disease.12 In such

| Study | OLT + MAL | Open MAL | MAL interv. | SA interv. | AHUG | HA to AA (no MAL interv.) | HA to AA + MAL interv. | HA to CA/SA + MAL interv. | HA recon. (GDA preserv) | HA recon. (GDA preserv) no MAL interv. |
|-------|-----------|----------|--------------|------------|------|--------------------------|------------------------|--------------------------|------------------------|--------------------------------------|
| Ali and Patel21 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cassar et al8 | 1 | 1 | no | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Czigany et al8 | 34 | 28 | 1 | 3 | 2 | 0 | 0 | 0 | 27 | 2 |
| Demian et al15 | 30 | 10 | NA | 16 | 0 | 0 | 0 | 0 | 10 | 4 |
| Golse et al9,10 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Jurim et al13 | 17 | 17 | 0 | 2 | 0 | 0 | 0 | 4 | 1 | 12 | 0 |
| Kisaoglu et al12 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| Krobny et al10 | 1 | 1 | 0 | 0 | NA | NA | NA | NA | NA | NA |
| Lubrano et al10 | 10 | 1 | 0 | 4 | 0 | 0 | 0 | 0 | 1 | 5 |
| Mochizuki et al8 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| Rodriguez-Garcia et al17 | 1 | 0 | 0 | 0 | NA | NA | NA | NA | NA | NA |
| Sun et al10 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| Vandermeulen et al2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| Vilatoba et al9 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| Woodworth et al25 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 |
| Fukuzawa et al12 | 5 | 3 | 0 | 2 | 0 | 0 | 0 | 0 | 3 | 0 |
| Jiang et al23 | 1 | 1 | 0 | 1 | NA | NA | NA | NA | NA | 0 |
| Agnes et al13 | 5 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 0 |
| Sharafuddin et al16 | 1 | 0 | 0 | 0 | NA | NA | NA | NA | NA | NA |
| Uchida et al22 | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 |
| Hewitt et al24 | 2 | 1 | 1 | 2 | NA | NA | NA | NA | NA | NA |

AA, accessory artery; AHUG, aortohepatic jump graft; CA, celiac artery; GDA, gastroduodenal artery preservation; HA, hepatic artery; interv., intervention; MAL, median arcuate ligament; no, not available; OLT, orthotopic liver transplant; SA, splenic artery; recon., reconstruction.
cases, a MAL-releasing procedure would be counterproductive, and an arterial jump graft would be more beneficial.

Various approaches have been suggested for releasing a MAL. These include an open or a laparoscopic approach and radiological stenting. The open approach (63.2%) during OLT seems to be the preferred option from our review. Hewitt et al. performed a laparoscopic hand-assisted MAL intervention 4 mo after OLT (Figure 2).

Percutaneous angioplasty and stenting across the celiac trunk is an option but could prove fatal if thrombotic occlusion or stent crushing due to repetitive compression stresses occurs. Furthermore, there is a requirement for long-term post-procedure therapeutic anticoagulation. Sharafuddin et al. mention radiological stent placement across celiac axis post-OLT due to deranged liver function. In their report, a second endovascular stent was placed to improve the liver function, but there was a persistent moderate residual arterial stenosis.

Various complications have been reported because of MAL release, which includes injury to surrounding structures and pancreatic fistula. Our review noted a low rate of celiac artery injury (2.6%), stenosis (3.9%), liver infarction (2.4%), and thrombosis (2.6%) compared with 17% HA thrombosis without MAL release.

Given the current variability in diagnosis, reporting, and treatment options, many of which are implemented during a subsequent operation postliver transplant, we suggest that there is a need for a better diagnosis and an increased index of suspicion of MAL if there are noticeable differences in the arterial flow intraoperatively at the time of transplant with respiration. We, therefore, suggest that the hepatic arterial flow changes with the respiratory cycle should be assessed. If the intraoperative arterial flow after clamping the recipient gastroduodenal artery is poor with no variation with respiration and no evidence of aortoiliac atherosclerosis, an aortic jump graft should be considered as the primary approach. If, however, there is a clear flow variation on respiration (30%–50% drop), the arterial inflow should be established, preserving the additional inflow from the recipient GDA. If the flow remains poor, an open MAL release should be attempted, and failing that, an aortic jump graft should be considered (Figure 2). If the initial flow achieved is sufficient to ensure good graft vascularity, a delayed laparoscopic MAL release or radiological stenting of the celiac axis can be undertaken, to ensure long-term patency.

There are several limitations to the present systematic review. There is great heterogeneity and paucity of data on the topic with a small number of studies presenting different approaches. Furthermore, the quality of the published reports varies from poor to good, and as such, pooling of data may cause an inherent bias. Although the proposed algorithm...

![FIGURE 2. A suggested algorithm for intraoperative HA flow assessment during liver transplantation. GDA, gastroduodenal artery preservation; HA, hepatic artery.](image)
attempts to provide some structure to the clinical decision making and to improve future reporting, it is based on what has been reported to date, and as such, it may need further refinement as more consistent data are reported.

In summary, the presence of a MAL is under-reported in the setting of liver transplantation, in which it can have devastating consequences for the graft. A preoperative diagnosis or a high index of suspicion should trigger a structured approach to ensure excellent vascular supply to the graft with minimal associated morbidity.

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