Dual Graft Living Donor Liver Transplantation for High Acuity Patients: A Single-Center Experience

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Background: **The outcomes of dual graft living donor liver transplantation (DGLDLT) in high acuity patients remain underreported. The objective of this study was to report long-term outcomes from a single center in this select group of patients.** ***Methods:*** **This was a retrospective review of patients who underwent DGLDLT between 2012 and 2017 (n = 10). High acuity patients were defined as patients with model for end stage liver disease (MELD) ≥30 or Child Pugh score ≥11. We looked at 90-day morbidity and mortality and 5-year overall survival (OS).** ***Results:*** **The median MELD score and Child Pugh score were 30 (26.7–35) and 11 (11–11.2). The median recipient weight was 105 (95.2–113.7) and ranged from 82 to 132 kg. Out of 10 patients, 4 (40%) required perioperative renal replacement therapy, and 8 (80%) required hospital admission for optimization. The estimated graft to recipient weight ratio (GRWR) with right lobe graft alone was <0.8 in all patients, between 0.75 and 0.65 in 5 (50%) patients, and <0.65 in 5 (50%) patients. The 90-day mortality was 3/10 (30%), and there were 3/10 (30%) deaths during long-term follow-up. Among 155 high acuity patients, the 1-year OS with standard LDLT, standard LDLT with GRWR <0.8, and DGLDLT was 82%, 76%, and 58%, respectively (*P* = 0.123). With a median follow-up of 40.6 (1.9–74.4) months, the 5-year OS for DGLDLT was 50%.** ***Conclusion:*** **The use of DGLDLT in high acuity patients should be prudent and low GRWR grafts should be considered a viable alternative in selected patients.** **(J Clin Exp Hepatol 2023;13:447–453)**

Liver transplantation

Living donor liver transplantation (LDLT) is a feasible option in regions with limited deceased donor liver transplant (DDLT) activity.[1] Superior graft quality, short ischemia times, and elective nature of surgery, before development of life threatening complications, makes LDLT a useful option for liver transplantation.[2,3] However, ensuring adequate future liver remnant (FLR) in the donor and graft weight in the recipient is a challenge unique to LDLT.

The minimum acceptable graft to recipient weight ratio (GRWR) to avoid small for size syndrome (SFSS) in LDLT is ≥ 0.8, while the FLR in donors should be 30%.[4] In patients with high body mass index (BMI), finding an ideal donor can be a difficult proposition. Ensuring an FLR >30% in the donor to avoid posthepatectomy liver failure (PHLF) and adequate graft mass in the recipient to avoid SFSS is critical for safe LDLT.[5–7] In this context, dual graft LDLT (DGLDLT) was proposed where two living donors donate a portion of their liver and collectively achieve the required GRWR for one patient.[8,9] As a result, LDLT can be considered for a patient who would not be transplantable otherwise, particularly in regions with limited DDLT activity. Keeping in mind the value of donor safety and well-being, an argument can be made against risking two donors to save one life. However, with this approach, smaller grafts are procured from donors, thereby enhancing donor safety and reducing the risk of posthepatectomy liver failure.[10]

Despite its potential advantages, DGLDLT has not gained widespread acceptance due to its technical complexity, limited feasibility, and narrow spectrum of indications. Outside Korea and Japan, DGLDLT has remained an infrequently considered liver transplant option.[5] With accumulating evidence supporting the safe use of grafts with GRWR <0.8 in LDLT, the indications of DGLDLT are likely to remain limited.[11] At our center, a GRWR ≥0.6 is considered acceptable for most patients, and DGLDLT is only considered for patients who are sick with high model for end stage liver disease (MELD) scores.

The objective of the study was to report 5-year outcomes of DGLDLT in high acuity patients at our center.

Keywords: dual graft living donor liver transplantation, graft to recipient weight ratio, mortality, posthepatectomy liver failure, small for size syndrome

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Abbreviations: ACLF: Acute on chronic liver failure; CRRT: Continuous renal replacement therapy; DCLD: Decompensated liver disease; DGLDLT: Dual graft living donor liver transplantation; FLR: Future liver remnant; GRWR: Graft to recipient weight ratio; PHLF: Posthepatectomy liver failure; SFSS: Small for size syndrome

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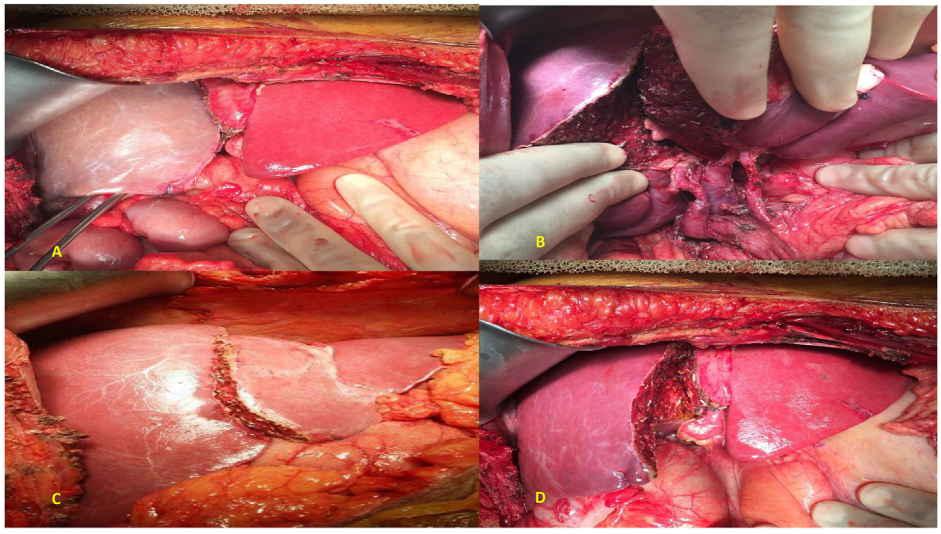

Figure 1 Various steps and types of DGLDLT (a) The left lobe graft has been reperfused before right lobe implantation (b) Both the right and left lobe grafts perfused (Note the replaced right hepatic artery from superior mesenteric artery for the right lobe arterial inflow) (c) DGLDLT with right lobe and left lobe graft (d) DGLDLT with right lobe and left lateral sector graft. DGLDLT, Dual graft living donor liver transplantation.

METHODS

Study Population

This was a retrospective review of patients who underwent DGLDLT between April 2012 and November 2017. During the study period, 434 LDLTs were performed at our center. There were 155 adult patients with MELD ≥30 or Child Turcot Pugh (CTP) ≥11 C. Out of these, 121 patients had standard LDLT with GRWR >0.8, 24 patients had LDLT with GRWR <0.8, and 10 patients had DGLDLT. In addition, one more patient underwent DGLDT but did not meet the high acuity criteria. Ten patients with a MELD score ≥30 or CTP score ≥11 were included (high acuity). A DGLDLT was considered when GRWR was <0.7 in high MELD patients and a suitable second donor was available. The donor and recipient evaluation and selection have been discussed in detail elsewhere.[1,12]

Surgical Procedure and Graft Selection

The surgical procedure was performed simultaneously on the donors and recipient sides. On the recipient side, laparotomy was followed by division of the triangular ligaments to mobilize the left and right lobes of the liver. A high hilar dissection was performed at the porta hepatis, all major lymphatics were ligated, and the RHD and LHD were divided. Similarly, the hepatic arteries were divided as high as possible. Portal vein was skeletonized, and a temporary portocaval shunt was performed between the right portal vein and the supra renal inferior vena cava (IVC). The liver was filleted off the IVC by transfixing the caudate veins and the right (RHV) was clamped and divided. The middle hepatic vein (MHV) along with the left hepatic vein (LHV) was clamped using a Satinsky clamp, and recipient hepatectomy was completed.

Right Lobe Graft Implantation

The right lobe graft was implanted first. The posterior wall of the graft's right hepatic vein (RHV) was anastomosed with the recipient's RHV vein stump. The liver was flushed with normal saline via the portal vein. At the end of the flush, the anterior wall of the RHV anastomosis was completed. At our center, we reconstruct all substantial anterior sector veins. In fact, more than 70% of our patients have anterior sector venous reconstruction.[13,14] In DGLDLT, Segment 5 and 8 veins were usually not reconstructed due to our preference for RHV-dominant anatomy in majority of right lobe grafts. The right portal vein (RPV) of the graft was anastomosed the RPV of the recipient. The patient was checked for hemodynamic stability before the clamps were removed, first from the hepatic vein, followed by the portal vein. The donor's RHA hepatic artery was anastomosed to right hepatic artery of recipient. Intraoperative Doppler US was performed to confirm flow and velocities.

Implantation of Left Lobe Graft

The combined orifice of the middle hepatic vein (MHV) and left hepatic vein (LHV) with caval extension was anastomosed with the LHV or the LHV/MHV of the left lobe. The left portal vein (LPV) of the left lobe graft was anastomosed to LPV of recipient. The left hepatic artery (LHA) was anastomosed to the LHA of the recipient. The choice between left lateral and left lobe graft was based on multiple factors including final GRWR (GRWR >0.8), anatomy, quality of graft, and whether segmental veins on the cut surface required reconstruction. Figure 1 shows various types of DGLDLT performed at our center.

Table 1 Patient Characteristics.

Recipient factors	Number (%) (n = 10)
Demographics	
Male gender	10 (100)
Weight in kg, median (IQR)	105 (95.2–113.7)
BMI, kg/m^2, median (IQR)	32.6 (31.6–34.3)
Extent of liver failure	
MELD, median (IQR)	30 (26.7–35)
CTP score, median (IQR)	11 (11–11.2)
Perioperative CRRT	4 (40)
Pretransplant hospital stay	8 (80)
Etiology	
HBV related ESLD	1 (10)
HCV related ESLD	3 (50)
Alcohol related ESLD	1 (10)
NASH related ESLD	2 (20)
Acute on chronic liver failure	3 (30)
Hepatocellular carcinoma	3 (30)
Donor's relation with the recipient	(n = 20)
Son	5 (25)
Nephew	2 (10)
Sister	2 (10)
Niece	2 (10)
Daughter	6 (30)
Sister-in-law	1 (5)
Cousin	2 (10)

BMI, Body mass index; CIT, Cold ischemia time; CRRT, Continuous renal replacement therapy; CTP, Child Turcot Pugh; ESLD, End stage liver disease; ERCP, Endoscopic retrogarde cholangiopancreatography; GRWR, Graft to recipient weight ratio; HBV, Hepatitis B virus; HCC, Hepatocellular carcinoma; HCV, Hepatitis C virus; ICU, Intensive care unit; IQR, Interquartile range; MELD, Model for end stage liver disease; MHV, Middle hepatic vein; NASH, Non-alcoholic steatohepatitis; PTC, Percutaneous tranhepatic cholangiography; WIT, Warm ischemia time.

The duct-to-duct biliary anastomoses for the right and left grafts were performed as the last step. Occasionally, a Roux-en-Y loop hepaticojejunostomy was required for the left lobe. Portal pressure was not checked since the decision to perform DGLDLT was based upon preoperative parameters and both donor operations started simultaneously and therefore were unlikely to change the decision to perform DGLDLT.

Statistical Analysis

The complications were reported based on Clavien-Dindo grading.[15] Data analysis was done on SPSS (Statistical Package for the Social Sciences) software version 28.0.1.1. Categorical data were presented as frequency and percentage, while continuous data were presented as medians with interquartile range. Survival was calculated by subtracting the date of death or last follow-up from date of transplant. Kaplan–Meier curves were

Table 2 Graft-Related Variables, Major Complications and Mortality in DGLDLT Recipients.

Graft and operative variables	Number (%) (n = 10)
Graft type (n = 20)	
Right lobe graft without MHV	9 (45)
Right lobe graft with partial MHV	1 (5)
Left lobe graft	7 (35)
Left lateral sector	3 (15)
Operative details	
Combined GRWR, median (IQR)	1 (0.9–1.2)
Right lobe WIT, minutes, median (IQR)	30 (28–46)
Right lobe CIT, minutes, median (IQR)	29 (14.7–45)
Left lobe WIT, minutes, median (IQR)	36 (33.7–41.5)
Left lobe CIT, minutes, median (IQR)	26.5 (15–46.5)
Operative time, minutes, median (IQR)	750 (720–912)
Blood loss, ml, median (IQR)	2750 (1900–7000)
Major complications	
Grade 3	
Intra-abdominal collection (aspiration under US)	2 (20)
Bile leak (PTC)	1 (10)
Biliary stricture (ERCP and stent placement)	2 (20)
Pleural effusion (aspiration under US)	3 (30)
Grade 4	
Respiratory failure (re intubation)	2 (20)
Renal failure (Renal replacement therapy)	3 (30)
Septic shock (readmission in ICU)	7 (70)
Days in hospital	
Postoperative ICU stay, median (IQR)	6.5 (4.7–20.2)
Postoperative hospital stay, median (IQR)	22.5 (16.2–40.5)
Short-term mortality	
Chest hemorrhage after tube thoracostomy	1 (10)
Pneumonia leading to respiratory failure	1 (10)
CRRT-related septic shock	1 (10)
Long-term mortality	
Myocardial infarction	1 (10)
Dialysis-associated shock	1 (10)
Unknown	1 (10)

CIT, Cold ischemia time; CRRT, Continuous renal replacement therapy; ERCP, Endoscopic retrogarde cholangiopancreatography; GRWR Graft to recipient weight ratio; ICU Intensive care unit; IQR, Interquartile range; MHV, Middle hepatic vein; PTC, Percutaneous tranhepatic cholangiography; WIT, Warm ischemia time.

used to calculate 5-year survival. Specifically, we looked at 90-day and long-term mortality.

RESULTS

Patient Characteristics

The median age was 54 (35–59) years, and all patients belonged to the male gender. The median recipient weight was 105 (range = 82–132) kg as shown in Table 1. Out of 10 patients, 4 (40%) required continuous renal replacement therapy (CRRT) in the perioperative period. Preoperative CRRT was needed in two patients with renal dysfunction and one patient with chronic renal failure. In addition, 8 (80%) patients required hospital admission for optimization before LT. The median hospital stay in these patients was 6.5 (3–19) days. Three patients with grade 3, EASL-CLIFF acute on chronic liver failure (ACLF) also underwent DGLDLT. These patients had underling HBV cirrhosis (n = 1), HCV cirrhosis (n = 1), and HBV-HCV cirrhosis (n = 1). Three patients had HCC; however, this was not the sole indication for LT in any of these patients. Majority of donors were first degree relatives of the recipient, that is, 13/20 (65%).

Operative Details and Outcomes

Table 2 shows the graft and operative variables in patients who underwent DGLDLT. Overall, 8/10 (80%) patients had major complications. There was no graft related short-term or long-term mortality. The 90-day mortality was 3/10 (30%). In addition, there were three deaths during follow-up. These were due to myocardial infarction (n = 1) 63 months after transplant, hemodialysis associated shock (n = 1) 18 months after transplant, and unknown reasons (n = 1) 8 months after transplant. The patient on dialysis had long-standing chronic renal failure many years before LDLT. The estimated GRWR with right lobe graft alone was <0.8 in all patients, between 0.75 and 0.65 in 5 (50%), and <0.65 in five (50%) patients. Four patients (40%) were alive, while there was one mortality more than 5 years after DGLDLT as shown in Table 3. With a median follow-up of 40.6 (1.9–74.4) months, the 5-year overall survival was 50%. The 1-year overall survival in high acuity patients who underwent standard LDLT with GRWR ≥0.8, standard LDLT with GRWR <0.8, and DGLDLT was 82%, 76%, and 58%, respectively (P = 0.123) (Figure 2).

Donor Details

Among 20 donors, median age was 22.5 (20–28.7) years, and male to female ratio was 1:1. The median BMI was 23.7 (21.1–24.8) kg/m^2. Median liver attenuation index (LAI) was 13.5 (12–16.7). Variant portal anatomy was seen in two donors. The median operative blood loss was 500 (500–800) ml. There was one grade 3 morbidity where a donor required aspiration of abdominal collection. There was no donor mortality.

DISCUSSION

The current study reports long-term outcomes in 10 high acuity DGLDLT recipients. The in-hospital mortality of 30% and 5-year survival of 50% are lower than anticipated with standard LDLT. However, outcomes are reported in a selective group of patients who were very sick with high expected short-term mortality (3-month mortality = 50–80%) without transplant.[16]

The use of DGLDLT as a standard option to expand donor pool has met little enthusiasm. The largest experience has been reported from Korea, where more than 400

Table 3 Outcome in Patients Who Underwent DGLDLT.

Sex/Age/Blood group	BMI (kg/m^2)	Diagnosis	MELD/CTP score	Estimated right lobe GRWR	Estimated combined GRWR	Actual GRWR	Graft type	Outcome
M/35/O+	34.3	Alcohol related ESLD	35/10C	0.58	0.89	0.81	Right lobe + left lateral	In hospital mortality
M/55/O+	34.2	HCV, HCC, ESLD	26/13C	0.71	1.08	0.9	Right lobe + left lateral	Dead, 63 months
M/57/B+	32	NASH, ESLD	31/10C	0.68	1.12	0.9	Right lobe with partial MHV + left lateral	Alive, 81 months
M/48/B+	34.3	HCV, ACLF	35/10C	0.6	1.0	0.87	Right lobe + left lobe	Alive, 85 months
M/62/B+	34.9	HCV, HCC, ESLD	27/11C	0.68	1.01	1.05	Right lobe + left lobe	Dead, 18 months
M/54/O+	43.1	NASH, ESLD	17/12C	0.54	0.82	0.92	Right lobe + left lobe	In hospital mortality
M/49/O+	27	HBV, HCV, ACLF	37/10C	0.71	1.08	1.23	Right lobe + left lobe	In hospital mortality
M/35/O+	32.9	HBV, ESLD, DCLD	28/11C	0.61	0.9	0.98	Right lobe + left lobe	Alive, 71 months
M/32/A+	29.7	HBV, ACLF	34/11C	0.71	1.02	1.09	Right lobe + left lobe	Dead, 8 months
M/50/A+	28.5	HCV, HCC, ESLD	27/13C	0.55	0.88	1.22	Right lobe + left lobe	Alive, 67 months

ACLF, Acute on chronic liver failure; BMI, Body mass index; CTP, Child Turcot Pugh; ESLD, End stage liver disease; GRWR, Graft to recipient weight ratio; HBV, Hepatitis B virus; HCC, Hepatocellular carcinoma; HCV, Hepatitis C virus; MELD, Model for end stage liver disease; NASH, Non-alcoholic steatohepatitis.

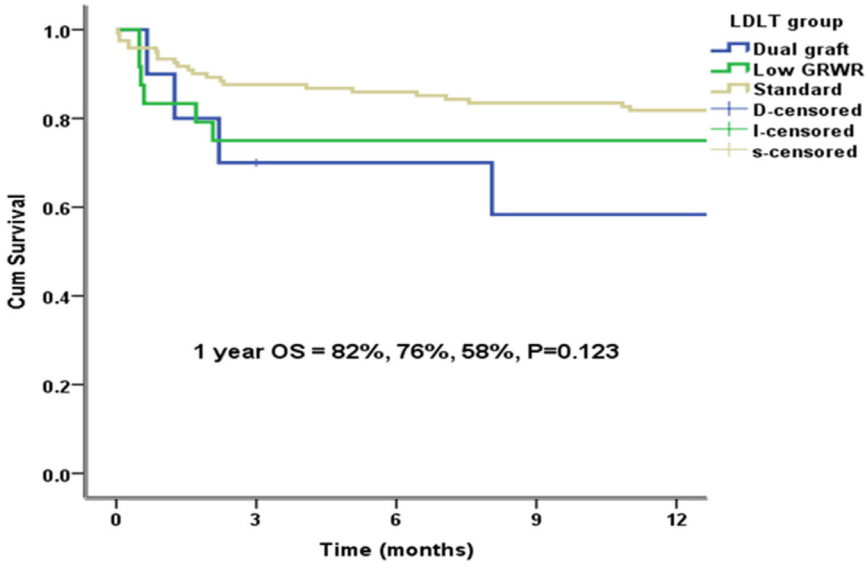

Figure 2 The 1-year overall survival in high acuity patients who underwent LDLT with GRWR ≥0.8 (n = 121), LDLT with GRWR <0.8 (n = 24), and DGLDLT (n = 10).

DGLDLTs have been performed. The short-term and long-term outcomes were comparable with standard LDLT. The authors reported 1- and 5-year survival of 89.2% and 85.5%. The surgical morbidity was 53.7% in DGLDLT and 28.5% in standard LDLT (P < 0.001). Various combinations of right and left grafts were used and majority of patients had low MELD scores (mean = 20.6 ± 10.6). On multivariate analysis, MELD >30 was an independent predictor of mortality.[17]

Outside Korea, the experience with DGLDLT has remained limited and infrequently includes patients with high MELD and CTP scores. At our center, the lower limit of acceptable estimated GRWR is ≥ 0.6. Consequentially, very few patients qualify for DGLDLT. More specifically, a GRWR of 0.8 is considered essential in patients with acute liver failure, grade 2–3 acute on chronic liver failure, MELD ≥30, or CTP score ≥11. In these patients if the required GRWR is not achieved from a single donor, DGLDLT was considered. All patients who received DGLDLT were overweight (BMI >25 kg/m^2), and 7/10 (70%) (BMI >30 kg/m^2) were obese. Four patients required perioperative CRRT, eight patients required hospital admission for optimization before LT, and all patients had a MELD score of 30 or CTP score of 11 or greater at the time of transplant. Short-term mortality was not attributable to graft related complications and was due to frailty and body habitus.

Dual graft LDLT is a technically challenging procedure. The ethical and medical aspects of donor safety where two living donors donate for one patient coupled with technical complexity of dual graft implantation raises several concerns.[18] It has been shown that despite low morbidity and near zero mortality, a number of donors have untoward experiences after surgery.[19] A high hilar dissection with preservation of the length of hepatic arteries, portal vein branches, and bile ducts is crucial in DGLDLT. Complex vascular reconstructions and multiple arterial anastomosis are required in DGLDLT. More specifically, the surgical risk in two donors needs to be balanced with the likely outcome in high-risk patients. Given this complexity, majority of data on dual graft LDLT have traditionally been limited to case reports.[20–28] While we achieved 5-year survival of 50%, which is the minimum acceptable benchmark in LDLT, outcomes can be improved with better patient selection. The long-term outcomes can be improved if late deaths can be prevented. Late deaths were attributable to underlying comorbids such as renal failure, high BMI, and sedentary life style in the current study. Based on limited existing data, it is difficult to establish guidelines for DGLDLT, let alone in high-risk patients.

Regarding technical variations, we preferred sequential over simultaneous reperfusion due to anticipated long warm ischemia time for the right lobe graft with simultaneous reperfusion. Different centers have used different strategies. For example, at Asan medical center, the choice of sequential versus simultaneous reperfusion was dependent on the combination of grafts used for DGLDLT. Sequential reperfusion was performed with two left lobe grafts, while simultaneous reperfusion was preferred in patients with a right and left lobe combination.[17]

It was shown that in hospital mortality in patients with MELD >30 or in patients requiring renal replacement therapy was 17.1% and 28.6%. Similarly, the 1-year survival was 79.2% and 65.5%, respectively.[17] We have shown that in-hospital mortality in our high acuity DGLDLT patients was 30%, and 1-year survival was 58%. This high mortality

reported with DGLDLT questions the utility of DGLDLT in high-risk patients. Moreover, we have shown that during the same time period, the 1-year survival with standard LDLT with low GRWR grafts was 76% in high acuity patients. In fact, it has been shown that low GRWR can be safely used in high-risk patients with or without portal flow modulation.[11] However, for low GRWR grafts to be acceptable, they have to be of high quality. In an urgent setting with high MELD patients, donors with borderline BMI (>30 kg/m^2), and graft steatosis (10–30%), low GRWR grafts might not be a viable alternative. DGLDLT might be a useful salvage option in these cases. This is reflected in our practice as well, and we have not performed DGLDLT since 2017. With increasing reliance on low GRWR grafts, the lowest acceptable GRWR, particularly in high-risk patients remains to be determined.

With a substantial increase in surgical complications and concerns regarding donor safety, DGLDLT is likely to remain an infrequent technique to expand donor pool. While there is no doubt that DGLDLT can be useful in selected cases, its indications remain less clearly understood, and its use in high-risk patients merits further exploration.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

AK and FA contributed to design, concept, data collection and manuscript writing.

FSD and NAK contributed to the concept and critical review.

AHB contributed to design, concept, data analysis, manuscript writing and critical review.

All authors approved the final version to be published.

CONFLICTS OF INTEREST

All authors have none to declare.

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