New onset atrial fibrillation during orthotopic liver transplantation induced by iced saline injection for transpulmonary thermodilution: a case report

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Abstract
Transpulmonary thermodilution is often used to measure extravascular lung water during liver transplantation. Here, the case of new onset atrial fibrillation during orthotopic liver transplantation, which may have been induced by iced saline injection for transpulmonary thermodilution measurement, is described. A 52-year-old male patient underwent orthotopic liver transplantation due to alcoholic cirrhosis combined with portal hypertension. During dissection of the recipient liver, transpulmonary thermodilution was performed. At 3 minutes following iced saline injected, atrial fibrillation occurred, the ventricular rate increased to more than 120 beats per min, and blood pressure dropped to 75/50 mmHg. Massive haemorrhage, inferior vena cava clamping, electrolyte disorder, acid-base balance disorder, and hypothermia were all ruled out, and iced saline injection was suspended. Hemodynamic stability was maintained with phenylephrine and lanatocide C (cedilanid), and chemical cardioversion was performed using amiodarone. During the reperfusion phase, transient hemodynamic instability was managed by norepinephrine. The neohepatic phase was uneventful. Atrial fibrillation lasted for 5 days and reversed to sinus rhythm automatically. The patient was hemodynamically stable during this period, and recovery was smooth with no thromboembolic events. In conclusion, atrial fibrillation may be induced by iced saline injection for transpulmonary thermodilution measurement during orthotopic liver transplantation.

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**Introduction**

Liver transplantation remains the primary method for treating end-stage liver diseases, however, up to 47% of patients develop pulmonary oedema after the procedure. Pulmonary oedema can be divided into two subtypes: hydrostatic, with intravascular volume overloading; and nonhydrostatic, with increased pulmonary capillary permeability. Extravascular lung water (EVLW) and pulmonary vascular permeability index (PVPI) may be measured using transpulmonary thermodilution (TPTD), and when combined, can be helpful in diagnosing, assessing severity, and guiding therapy in cases of pulmonary oedema. In addition, increased EVLW and PVPI has been associated with prolonged mechanical ventilation (>48 h) after liver transplant. Furthermore, higher pretransplant EVLW and PVPI levels have been associated with postoperative acute lung injury in living donor liver transplant patients. Finally, TPTD may also be used to measure the cardiac index and global end diastolic volume, both of which may be used to guide fluid management in critically ill patients. Therefore, use of TPTD in the perioperative period during liver transplantation has certain benefit.

Transpulmonary thermodilution requires the injection of a bolus of iced indicator into the superior vena cava. The thermodilution curve in the aorta is detected by a femoral artery catheter with a thermistor at the tip. By analysing the thermodilution curve, the EVLW, PVPI, cardiac index and global end diastolic volume are intermittently measured, and by analysis of the arterial curve sampled through the arterial catheter, the real-time cardiac index is also measured. Herein, the case of a patient who experienced new onset atrial fibrillation (AF) during orthotopic liver transplant, which may have been induced by iced saline injection for TPTD measurement, is described. To the best of our knowledge, AF is a rare complication induced by iced saline injection during liver transplantation.

**Case report**

This work was approved by the Ethics Committee of the First Affiliated Hospital of Xi’an Jiaotong University. Written informed consent to treatment and to publish the case was obtained from the patient. The reporting of this case report conforms to CARE guidelines.

**General patient information**

A 52-year-old male patient (height, 169 cm; weight, 70 kg) underwent orthotopic liver transplantation at the First Affiliated Hospital of Xi’an Jiaotong University, Xi’an, China in March 2021, due to alcoholic cirrhosis combined with portal hypertension. The patient had undergone percutaneous transhepatic esophagogastric vein occlusion for upper gastrointestinal bleeding four years previously. He had no history of AF. Preoperative transthoracic echocardiography showed decreased...
relaxation function of the left ventricle, with ejection fraction of 51%, while the left atrium (LA) and right atrium (RA) sizes were within normal range (LA, 26 mm x 30 mm; RA, 30 mm x 35 mm). Preoperative electrocardiogram (ECG) showed sinus rhythm with a heart rate of 72 beats per min (bpm). The chest computed tomography scan showed right pleural effusion and ooze in the right lower lobe. Abdominal ultrasound showed massive ascites. The patient had mild anaemia with haemoglobin level of 102 g/L, coagulopathy with platelet count of 24 x 10⁹/L, fibrinogen level of 1.58 g/L, prothrombin time of 17.1 s, and activated partial prothrombin time of 46.1 s. He also had hypokalaemia with serum potassium concentration of 3.03 mmol/L. The Child–Pugh score was class C, the model for end-stage liver disease (MELD) score was 22, and the CHA2DS2VASc score was 0.8.9

Anaesthesia and monitoring

Five-lead ECG, blood oxygen saturation, femoral arterial blood pressure (BP), central venous pressure, nasopharyngeal temperature, and bispectral index were monitored. Anaesthesia was induced by intravenous (i.v.) administration of 2 mg midazolam, 14 mg etomidate, 25 µg sufentanil and 50 mg rocuronium. Anaesthesia was maintained by i.v. administration of 4–8 mg/kg/h propofol and 0.1–0.5 µg/kg/min remifentanil, plus 0.5–1% sevoflurane by inhalation. The bispectral index level was maintained between 40–60. Rocuronium (20 mg, i.v. injection) was intermittently administered for muscle relaxation. A protective ventilation strategy was adopted, with a tidal volume of 6 ml/kg, inhaled oxygen concentration of 40–60%, positive end expiratory pressure of 5–10 cmH₂O, and end expiratory carbon dioxide maintained between 35 and 45 mmHg.

Potassium chloride and calcium gluconate were infused to maintain serum potassium concentration >3.5 mmol/L, and serum free calcium concentration >1 mmol/L. Sodium bicarbonate was used to correct metabolic acidosis. Fresh frozen plasma, cryoprecipitate, platelets, fibrinogen, and prothrombin complex were used to correct coagulopathy according to the thromboelastogram. Red blood cells were transfused to maintain the haemoglobin level >80 g/L.

TPTD measurement

Following anaesthesia induction, a central venous catheter was placed in right internal jugular vein. A thermosensitive catheter was placed in the right femoral artery; this catheter has a thermistor connected to a EV1000/VolumeView™ system (Edwards Lifesciences, Irvine, CA, USA) for TPTD measurement, plus an additional lumen for measuring arterial BP. TPTD was performed by bolus iced saline injection (<8°C, 15 ml) through the central venous catheter. The saline was injected manually and always completed within 3 s, and the mean of three consecutive iced saline injections was calculated to increase the reliability of the measurement.

The new onset AF and rescue process

As described above, TPTD was performed after induction of anaesthesia. Following each iced saline injection, there was a slight drop in arterial BP. The cardiac index was 2.5 L/min/m², global end diastolic volume was 1121 ml, EVLW was 10 ml/kg, and PVPI was 2.4. To counter this, 20 mg furosemide (i.v. injection) was administered. During dissection of the recipient liver, TPTD was repeated. After each iced saline injection, there was a sharp drop in arterial BP combined with decreasing heart rate. Thus, 8 µg norepinephrine was administered by i.v. injection to maintain hemodynamic stability.
Blood gas analysis showed that electrolytes were within normal range and there was no acid–base balance disorder. Three minutes later, the ECG displayed AF, the ventricular rate increased to >120 bpm, and arterial BP dropped to 75/50 mmHg. Massive haemorrhage and inferior vena cava clamping were ruled out. 100 µg phenylephrine (i.v. injection) was repeatedly administered, and 0.4 mg lanatocide C (cedilanid; i.v. injection) was administered over 10 min to maintain hemodynamic stability. When the ventricular rate dropped to 95 bpm, arterial BP increased to 110/70 mmHg, and 150 mg amiodarone (i.v. injection) was administered over 10 min, followed by infusion at 1 mg/min. During the anhepatic phase of 45 min duration, phenylephrine was infused at 1–5 µg/kg/min. During the reperfusion phase, transient hypotension was reversed by repeated administration of 8 µg norepinephrine (i.v. injection). Use of epinephrine and dopamine was avoided due to concerns about rapid ventricular rate. The neohepatic phase was uneventful. The trends in electrolyte and acid-base balance changes during the operation are shown in Figure 1.

Transpulmonary thermodilution measurement was discontinued after onset of AF. Amiodarone was administered by intravenous infusion at 1 mg/min for 6 h, then at 0.5 mg/min for a further 18 h, and no anticoagulant therapy was performed. AF lasted for 5 days, and reversed to sinus rhythm automatically. The ventricular rate was between 75–100 bpm and arterial BP was stable during this period. The transplant operation lasted for 8 h, after which, the patient was transferred to the intensive care unit (ICU) and the tracheal tube was extubated after 6 h. After 5 days in the ICU, the patient was transferred to a hospital ward where he exhibited a smooth recovery and was discharged after 20 days. There were no thromboembolic events.

**Discussion**

The intraoperative occurrence of arrhythmia is clinically important because it may lead to significant hemodynamic instability,10 with AF being the most common supraventricular arrhythmia that increases morbidity and mortality after an operation. Patients who undergo liver transplantation are frequently exposed to predisposing factors of AF. Most studies appear to focus on postoperative new onset AF, with few

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![Figure 1](image_url)

**Figure 1.** Trends in electrolyte and acid–base balance changes during orthotopic liver transplantation in a 52-year-old male patient with alcoholic liver cirrhosis and portal hypertension. T1, after anaesthesia induction; T2, new onset of atrial fibrillation; T3, anhepatic phase; T4, reperfusion phase; and T5, neohepatic phase. BE, base excess; k+, potassium; Ca2+, calcium; Na+, sodium.
studies reporting new onset AF during the operation itself. In one previously published study, the incidence of new onset AF during liver transplantation was reported to be 1.2%. Postoperative AF following liver transplantation has been shown to prolong the length of hospital stay, increase the incidence of acute kidney injury and the incidence of graft failure at 1 year, and was shown to be an independent risk factor for post liver-transplant mortality. Postoperative AF was also associated with an 8-fold increased risk of stroke and systemic embolism events over a median follow-up of 4.9 years.

Autonomic imbalance, surgical stress, elevated catecholamine level, pre-existing pericardial inflammation, and cardiac malfunction are all factors attributed to the development of AF during liver transplantation. Acidosis, hypo/hyperkalaemia, hypocalcaemia, hypoglycaemia, and hypothermia during liver transplantation may also induce AF, and higher MELD score and fulminant hepatic failure have been associated with the occurrence of intraoperative AF. Hypomagnesaemia is a well-recognized cause of cardiac arrhythmia. In a previously published report of two cases, a patient with hypomagnesaemia was reported to have developed AF during liver transplantation, and their rhythm reversed to sinus only after the hypomagnesaemia was corrected. Massive haemorrhage, hypotension and high-dose use of catecholamines during liver transplantation may also induce AF, therefore, new onset AF may often occur in the anhepatic phase, due to the increased demand for positive inotropic drugs during this phase.

In the present case, AF occurred during dissection of the recipient liver. Massive haemorrhage, electrolyte disorder and acid–base balance disorder were all ruled out, and the nasopharyngeal temperature was within normal range. AF occurred immediately after the bolus injection of iced saline and injection of 8 μg of norepinephrine. Although norepinephrine has been correlated with higher incidence of AF in general ICU patients, it is often used to maintain hemodynamic stability within enhanced recovery pathways following surgery, and reports of increased AF incidence with low dose norepinephrine during surgery are rare. Thus, we speculate that the new onset of AF in the present case was more likely to be induced by bolus iced saline injection.

There are various possible mechanisms for bolus iced saline injection to induce AF. First, a sudden influx of fluid may cause mechanical stretch of the atria, and this atrial stretch is known to be a main contributor of AF development. Secondly, marked hypothermia caused by influx of iced saline is known to be another possible contributor to the development of AF. Thirdly, an animal model study showed that iced injectate during thermodilution could directly cool the sinoatrial node. Cooling the sinoatrial node during iced bolus injection may decrease the heart rate and cardiac output, and the transient hemodynamic fluctuation may also lead to the occurrence of AF.

If iced saline injection is not tolerated during PTPD, room temperature saline may be used instead, and may be more convenient for both patients and medical staff. A study of 45 patients treated in the ICU showed that the evaluation of EVLW with room temperature injectate (21°C) significantly correlated with the use of iced injectate. Room temperature injectate (24°C) may also be used in critically ill patients, including those undergoing liver transplant, for assessing cardiac index and EVLW. A good agreement has been shown between room- and iced-temperature injectate, but cardiac index values may be slightly increased compared with iced injectate.

In patients with AF, cardiac output is probably less stable due to the variation in
right ventricular filling time and the variable stroke volume this generates, and the TPTD cardiac output measurement may be less precise. Thus, TPTD measurement in the present case was discontinued after onset of AF. When TPTD cannot be performed, lung ultrasound may be used as an alternative method. As a non-invasive bedside investigation, lung ultrasound may be used to judge EVLW, whereby the more B-lines in lung ultrasound, the more serious the EVLW.

Usually, new onset of AF during liver transplantation may be self-limiting, often lasting between 1 hour and 1 week. The main treatment includes maintaining hemodynamic stability and controlling ventricular rate. Cardioversion with a 100–200 joules biphasic shock may be attempted in cases of hemodynamic instability, and chemical cardioversion may be performed using amiodarone, calcium channel blockers, and beta-blockers. Anticoagulant therapy was not considered in the present case, due to the following factors: First, the consideration of postoperative bleeding risk; Secondly, the CHA2DS2VASc score of the patient was 0. CHA2DS2VASc score has been well validated in assessing the risk of thromboembolism associated with AF, and may also estimate the risk of stroke in patients with AF, with higher scores indicating a greater risk of stroke, so the risk of a thromboembolic event was considered to be low in the present case; and Thirdly, a previously published study showed that early anticoagulant therapy did not improve clinical outcomes in critically ill patients with new onset AF, and a systematic review didn’t support early anticoagulant therapy for new onset AF whilst patients are critically ill.

**Conclusion**

This report describes a case of new onset intraoperative AF that may have been induced by iced saline injection for TPTD measurement during orthotopic liver transplantation. Further research into the effects of iced saline injection during surgery is required to validate the present finding.

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**Author contribution**

ZG collected the data, analysed the aetiology and wrote the manuscript. XL collected the data and performed the anaesthesia. XW performed the anaesthesia. All authors read and approved the final manuscript.

**Data accessibility**

All data relating to this case report are included within this manuscript. Data are available from the authors upon reasonable request.

**Declaration of conflicting interests**

The authors declare that there is no conflict of interest.

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