Use of midodrine for treatment of chylopericardium after coronary artery bypass grafting

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Chylopericardium after cardiac surgery was first described by Thomas and McGoon in 1971.1 To our best knowledge, there are only 25 reported cases of chylopericardium after cardiac surgery in adults worldwide (Table 1). Current conservative treatment options for chylopericardium include low-fat diet, total parenteral nutrition, and octreotide. We report a case of chylopericardium after coronary artery bypass grafting that was successfully treated with midodrine, octreotide, and low-fat diet.

CASE REPORT
A 60-year-old Chinese man presented with stable angina. Coronary angiogram showed triple-vessel disease and he underwent coronary artery bypass grafting with left internal mammary artery and saphenous vein graft conduits. The left pleura was incised during left internal mammary artery harvest. Postoperative progress was uneventful and he was discharged 6 days later.

He presented 13 days later with a moderate left pleural effusion, which drained serous fluid. He presented 10 days later with exertional dyspnea. He was hemodynamically stable. A chest radiograph showed a widened mediastinum (Figure 1, A). A bedside transthoracic echocardiogram (TTE) revealed a large pericardial effusion 4.7 cm from the lateral right ventricular wall with no diastolic collapse. Chest computed tomography imaging showed a large 4.6-cm pericardial effusion and a moderate-sized left pleural effusion (Figure 1, B).

Percutaneous pericardiocentesis and pericardial drain insertion was performed. A total of 1.9 L of serous fluid was drained in the first day. Milky drain output was noted the next day. Biochemical analysis showed a triglyceride level of 2.72 mmol/L. Fluid cultures were negative, which confirmed sterile chyle.

He was started on a low-fat diet supplemented with medium-chain triglyceride oil and intravenous octreotide. Because the drainage was still milky with high output of 400 to 500 mL/d (Figure 2), oral Midodrine treatment was started. Drain output decreased and became serous after midodrine treatment was started. He was weaned off octreotide treatment. Pericardial drainage was 100 to 200 mL/d even after weaning off octreotide treatment. The drain was removed 20 days later after it was found to be blocked despite flushing. Serial TTE showed a small stable pericardial effusion. He was discharged home with oral midodrine and gradual resumption of normal diet. TTE 3 weeks postdischarge showed no recurrence of pericardial effusion. Institutional review board approval was not required. Informed consent was obtained from the patient for publication.

DISCUSSION
Etiology
Several mechanisms can contribute to chylopericardium after cardiac surgery. Pericardial lymphatic channels can be disrupted at various locations. Dissection of the posterior pericardium before encircling major vessels with surgical
| Reference            | Location of chyle | Procedure             | Age/sex | Management                                                                                   |
|----------------------|-------------------|-----------------------|---------|---------------------------------------------------------------------------------------------|
| Kansu et al, 1977    | Pericardium       | AVR                   | 53/F    | Partial pericardiectomy                                                                     |
| Weber et al, 1981    | Pericardium       | CABG                  | 55/M    | MCT diet                                                                                    |
| Rose et al, 1982     | Pericardium       | Infundibular muscular resection and closure of septal defect for severe PS | 20/F    | MCT diet and ligation of transected lymphatic vessel                                         |
| Wong et al, 1982     | Anterior mediastinum | CABG                 | 42/F    | MCT diet, persistent chyle drainage prompted thoracic duct ligation                          |
| Schiessler et al, 1984 | Pericardium     | CABG                  | 45/M    | Continuous drainage and MCT diet                                                            |
| Lee et al, 1987      | Pericardium       | CABG                  | 49/M    | TPN, MCT oil, ligation of supradiaphragmatic thoracic duct and Denver pleuroperitoneal shunt |
| Pellegrini et al, 1987 | Pericardium     | CABG                  | 60/M    | Ibuprofen                                                                                   |
| Bar-El et al, 1989   | Pericardium       | MVR                   | 39/F    | MCT diet                                                                                    |
| Sharpe et al, 1999   | Pericardium and pleura | CABG              | 63/F    | Initially pigtail catheter, continued normal diet and drained intermittently from pericardial catheter for 5 days. Pigtail pericardial drain removed and replaced with larger drain and left-sided pleural drain inserted, tunneled feeding line introduced into left subclavian vein. Postoperatively NBM with TPN |
| Narayan et al, 2007  | Pericardium       | CABG                  | 65/F    | MCT diet, octreotide, surgical clip of severed lymphatic duct in thymic area                 |
| Sachithanandan et al, 2008 | Pericardium and left pleura | CABG | 58/M    | TPN and MCT diet                                                                            |
| Chalooob et al, 2008 | Pericardium       | AVR                   | 50/M    | Oversew of bilateral divided thymic lobes                                                    |
| Szabados et al, 2011 | Pericardium       | CABG                  | 46/F    | MCT diet and SC octreotide                                                                  |
| Albage et al, 2011   | Pericardium       | On-pump CABG          | 74/M    | TPN, I.V. somatostatin, and ligation of thoracic duct in posterior mediastinum adjacent to diaphragm |
| Mundra et al, 2011   | Pericardium       | AVR                   | 54/M    | Pericardial window and thoracic duct ligation                                               |
| Cheng et al, 2013    | Pericardium       | AVR and CABG          | 59/M    | Fat-free diet                                                                               |
|                     | Pericardium       | AVR                   | 45/F    | Fat-free diet, MCT oil, and octreotide                                                      |
| Koutsogiannidis et al, 2013 | Pericardium     | ASD closure            | 36/F    | TPN and MCT diet                                                                            |
| Karaca et al, 2014   | Pericardium       | Ascending aorta replacement | 47/M   | TPN and I.V. somatostatin                                                                   |
| Niznansky et al, 2015 | Pericardium     | Pulmonary endarterectomy | 48/F  | TPN, surgical ligation of injured lymphatic vessel at left lobe of thymus, ligation of whole left thymic lobe, and sealed with tissue glue |

(Continued)
tapes can cause inadvertent injury to mediastinal lymph vessels.26

Another source of chylopericardium is the thymus, which is routinely divided to gain exposure to the aorta for cannulation. There are multiple small lymphatic channels, with reports of large aberrant lymphatic ducts in the thymic area. Electrocautery dissection is inadequate to prevent lymphatic leakage because lymph contains less coagulable material than plasma. Chyle leak from the divided thymic tissue could be a possible source of chylopericardium in our patient.

Management
Persistent chyle leak can cause dehydration, malnutrition, and delayed wound healing. Chylopericardium can cause cardiac tamponade, acute pericarditis, or chronic constriction. If untreated, chylopericardium is associated with a mortality rate of up to 50%.

There is no consensus on the management of chylopericardium after cardiac surgery. Most studies adopted an initial conservative approach, reserving surgical treatment for cases with persistently high drainage despite medical therapy. Dietary modification with low-fat diet and medium-chain triglyceride oil can be trialed. Total parenteral nutrition is also effective. Somatostatin and its analog, octreotide, have been used as adjuncts with favorable outcomes.27 They reduce lymph flow by inhibiting the secretion of gastrointestinal hormones and decreasing splanchnic blood flow. For cases refractory to medical therapy, various surgical options have been described (Table 1).

Evidence in the current literature indicates a risk of failure with conservative treatment. Dietary modification and parenteral alimentation were successful in 10 of 16 cases (62.5%). Somatostatin/octreotide was successful in 4 of 6 cases (66.7%). A multimodal treatment approach helps to improve the success of conservative treatment. Midodrine is an alpha-1 adrenergic agonist, which causes vasoconstriction of the lymph system. This might lead to decreased chyle flow. To our knowledge, there are only 2 reported cases of midodrine use for chyle leak.28,29 To our knowledge, this is the first study to use midodrine for treatment of chylopericardium. Midodrine was used as the mainstay treatment option in our patient because it is generally safe

| Reference                  | Location of chyle          | Procedure | Age/sex | Management                        |
|----------------------------|----------------------------|-----------|---------|-----------------------------------|
| Attia et al, 201621        | Pericardium and right pleura | CABG      | 62/M    | TPN, SC octreotide, pericardial window, diaphragm plication and supradiaphragmatic thoracic duct ligation |
| Lippmann et al, 201622     | Pericardium                | AVR       | 50/M    | MCT diet                          |
| Erkut et al, 201923        | Pericardium                | CABG      | 61/M    | TPN with low fat and MCT diet     |
| Borulu et al, 202024       | Pericardium                | CABG      | 62/M    | TPN                               |
| Chia et al, 202025         | Pericardium                | MVR       | 67/M    | TPN                               |

AVR, Aortic valve replacement; F, female; CABG, coronary artery bypass grafting; M, male; MCT, medium-chain triglyceride; PS, pulmonary stenosis; TPN, total parenteral nutrition; MVR, mitral valve replacement; NBM, nil by mouth; SC, subcutaneous; I.V., intravenous; ASD, atrial septal defect.

FIGURE 1. A, Chest radiograph depicting widened mediastinum. B, Computed tomography scan showing a large pericardial effusion measuring up to 4.6 cm in thickness with no collapse of the right ventricle, and a moderate-sized left pleural effusion.
and can be used in the outpatient setting, which improves cost effectiveness as well.

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