Delivery of cardiac resynchronization therapy via the left inferior phrenic vein: a case report

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Background	The successful implantation of cardiac resynchronization therapy (CRT) may be prevented by anatomical variations that preclude the delivery of clinically effective left ventricular (LV) pacing from within the coronary sinus (CS) or its tributaries. Failure of lead delivery, suboptimal LV capture thresholds, or intractable phrenic nerve capture with accompanying diaphragmatic twitch is often encountered. Commonly employed alternative approaches to LV lead delivery, including epicardial, trans-septal, or transapical pacing are associated with significant morbidity.
Case summary	A 74-year-old man with ischaemic heart disease, prior mitral valve repair, long-standing atrial fibrillation, and severe symptomatic LV systolic dysfunction, underwent single chamber pacemaker upgrade to a CRT defibrillator. It was found not to be possible to place a CS lead during the procedure. Biventricular pacing was accomplished by the delivery of a pacing lead through the left inferior phrenic vein (LIPV). Satisfactory LV capture thresholds were obtained with the avoidance of clinically significant diaphragmatic stimulation. Following implantation, a marked clinical response to treatment was observed with improvement in both heart failure symptoms and LV ejection fraction.
Discussion	The LIPV is known to drain into the inferior vena cava in around one-third of examined subjects. In these individuals, LV lead delivery through the LIPV may provide an alternate route for the delivery of resynchronization therapy. This approach to the implantation of CRT may be considered when pacing via the CS or its branches are not achievable.
Keywords	Cardiac resynchronization therapy • Left inferior phrenic vein • Coronary sinus lead placement • Left ventricular pacing • Case report

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Learning points
- The left inferior phrenic vein (LIPV) drains into the inferior vena cava in approximately one-third of individuals.
- The LIPV can provide a novel option for the delivery of a pacing lead for the purposes of cardiac resynchronization therapy (CRT).
- Left inferior phrenic vein lead delivery for CRT might be a considered option when satisfactory left ventricular pacing cannot be achieved via conventional coronary sinus lead delivery

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Introduction

Cardiac resynchronization therapy (CRT) is a widely used and effective treatment; known to improve morbidity and mortality in appropriately selected patients with heart failure.[1] The most challenging aspect of implantation continues to be placement of the coronary sinus (CS) lead. This contributes to a procedure failure rate of 7.5–10%. Difficulties in CS lead placement are often due to variations in CS anatomy or the failure to obtain satisfactory electrical parameters during left ventricular (LV) pacing.[2,3] Cases abandoned due to such constraints are commonly referred for surgical epicardial LV lead placement, requiring thoracotomy.[4] Additional strategies to overcome difficulties in CS lead placement during the index procedure would be a valuable asset.

Timeline

2004	Anterior myocardial infarction
2005	Coronary bypass grafting and mitral valve repair complicated by complete heart block, treated by single chamber pacemaker implantation
2016	New York Heart Association (NYHA) III with left ventricular (LV) ejection fraction 20%, right ventricular pacing burden of 90%
August 2016	Device upgrade to cardiac resynchronization therapy defibrillator—LV lead sited in inferior phrenic vein
September 2016	Follow-up in device clinic, subject reports improvement in breathlessness, and exercise capacity
June 2017	LV ejection fraction reported as 44%
August 2018	Stable clinical condition, NYHA 1–2 symptoms, satisfactory LV capture with 94% true biventricular pacing

Case presentation

A 74-year-old man with a single chamber ventricular pacemaker *in situ* was referred to our unit for consideration of CRT defibrillator implantation. He had a history of anterior myocardial infarction in 2004. He subsequently developed LV systolic dysfunction (LV ejection fraction 25%), NYHA 2 symptoms and severe mitral regurgitation on a background of prior long-standing atrial fibrillation. Coronary bypass artery grafting with mitral valve repair and support ring placement was undertaken in 2005. The procedure was complicated by perioperative complete heart block. A single chamber pacemaker had been implanted post-operatively and had been programmed VVIR 60–130.

In 2016, he reported NYHA Class III symptoms. Blood pressure was 110/70 mmHg and estimated glomerular filtration rate 50 mL/min/1.73 m^2. Right ventricular (RV) pacing burden was >90%.
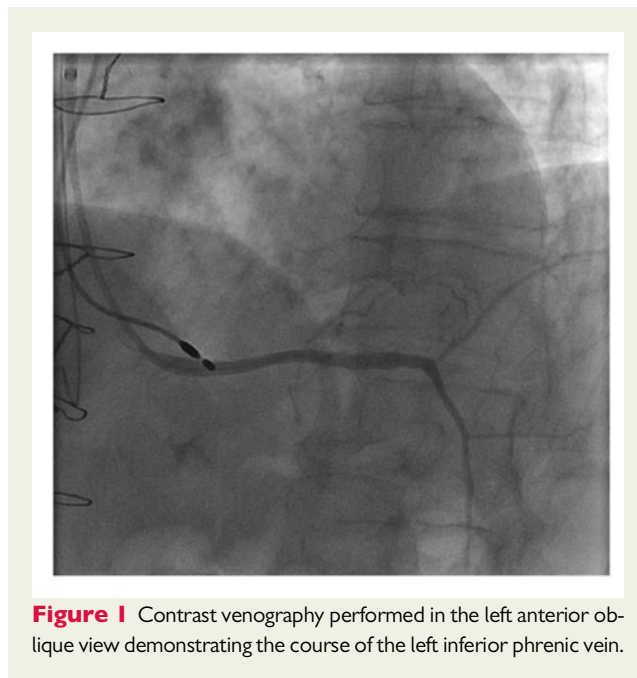
Figure 1 Contrast venography performed in the left anterior oblique view demonstrating the course of the left inferior phrenic vein.

Transthoracic echocardiography (TTE) demonstrated an LV ejection fraction of 20%. Medications included Irbesartan 150 mg od, spironolactone 25 mg od, warfarin, furosemide 40 mg twice daily, and hydralazine 25 mg three times daily. There were no symptoms of ischaemia and coronary artery angiography was not undertaken.

Implant details

At the time of device upgrade, venography demonstrated patent left upper limb venous conduits. The existing left pre-pectoral pocket was opened, and the left subclavian vein was punctured and double-wired. The CS ostium was not identified despite attempts by two experienced consultants. Guide catheters utilized included an Attain MB2, Attain EHXL, and Attain Deflectable (Medtronic). Inner catheters were used within each guide in a mother-child configuration. Catheters included an AL1, AL2, MPA, and JR4 (Cordis). At a fluoroscopy time of 40 min, the CS ostium had not been identified.

During attempts to localize the CS, the left inferior phrenic vein (LIPV) was unintentionally cannulated. This was noted to arise from immediately below the junction of the right atrium and inferior vena cava (IVC) (*Figure 1*). The mid-course of the vessel was noted to pass adjacent to the inferolateral LV wall.

On-table coronary artery angiography for CS localization, epicardial lead placement, and trans-septal lead placement were considered and discussed; however, the patient declined additional procedures. The possibility of using the LIPV for lead placement was discussed with the patient and he consented to proceed in the knowledge that a novel procedural approach, with incumbent risks, was being undertaken.

To progress the case, an RV defibrillator lead was fixed to the inferior ventricular septum. The LIPV was cannulated using an AL1 diagnostic catheter, introduced via the Attain deflectable guide catheter (Medtronic) and wired with a Whisper MS coronary guidewire (Abbott). An Attain Performa quadripolar pacing lead (Medtronic)
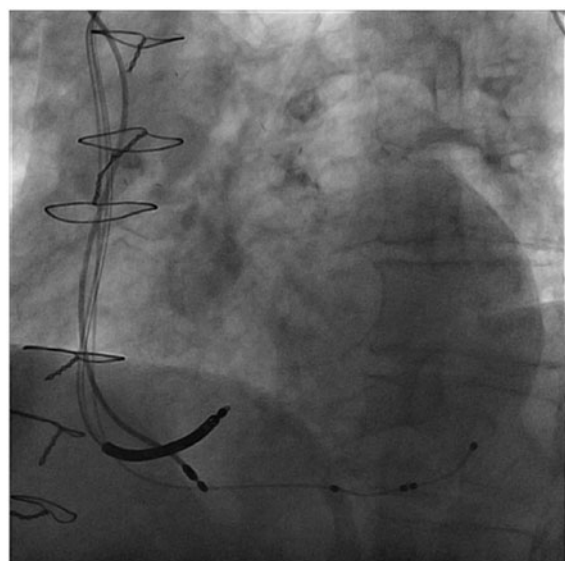
Figure 2 Final lead position as seen in the left anterior oblique view.
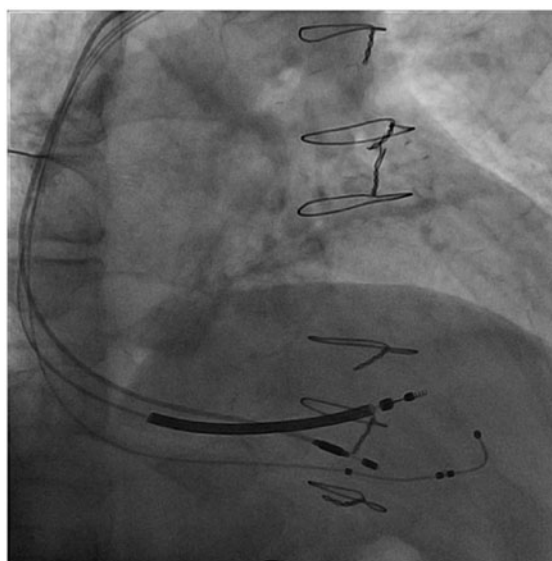
Figure 3 Final lead position as seen in the right anterior oblique view.

was passed to a site immediately adjacent to the inferolateral LV wall (*Figures 2* and *3*). LV capture thresholds and phrenic nerve capture thresholds were successfully assessed during pacing in a number of vector configurations (*Table 1*). The lead site was accepted, the device generator was implanted (Boston Scientific, Autogen CRT-D) and the procedure was concluded. Twelve-lead electrocardiograms showing native underlying rhythm, RV, and biventricular pacing following implantations are shown (*Figures 4–6*).

Clinical follow-up

At 6-week follow-up, the patient reported a marked improvement in breathlessness and improved exercise capacity. Phrenic nerve and LV capture vectors were assessed and found to be largely unaltered from the time of implantation (*Table 2*). Transthoracic echocardiography was repeated 10 months after the procedure and LV ejection fraction was reported to have improved, being 44%. Pacing parameters remained stable at follow-up of 22 months after the procedure (LV capture threshold of 2.5 V at pulse width 2 ms, June 2018). As of the current time (March 2019), the patient's clinical condition remains stable.

Discussion

Our centre is a university hospital providing tertiary care services to a population of 2.5 million. There are eight cardiac rhythm specialists and the centre implants in excess of 200 CRT devices per year. During CRT device placement, failure of implantation of an LV lead via the CS approach is not uncommon due to challenging anatomy, failure of satisfactory LV pacing, or intractable phrenic nerve capture. Surgical placement of an epicardial LV lead is historically the favoured alternative to CS lead placement. However, this necessitates an additional surgical procedure and thoracotomy.[5] Epicardial lead

Table 1   Left ventricular capture and diaphragmatic stimulation thresholds plus pacing impedances during device interrogation following implant

Left ventricular capture threshold (V)—at fixed pulse width of 2 ms

	LV-1	LV-2	LV-3	LV-4	RV coil	Can
LV-1		4	4	4	3.4	4
LV-2			6	5	4.5	3.4
LV-3		6		7	3.3	3.2
LV-4		6	6		7.5	3.5

Diaphragmatic stimulation threshold (V)—at fixed pulse width of 2 ms

	LV-1	LV-2	LV-3	LV-4	RV coil	Can
LV-1		1.5	2.8	2.5	3	1.7
LV-2			N	N	N	N
LV-3		N		6.5	N	N
LV-4		N	N		N	N

Lead impedance (ohms)

	LV-1	LV-2	LV-3	LV-4	RV coil	Can
LV-1		1016	1093	1093	653	673
LV-2			576	873	445	463
LV-3		533		782	396	413
LV-4		873	836		480	500

N = threshold >7.5 V.

placement may also be associated with infection, damage to the epicardial coronary arteries and may cause pericarditis leading to pericardial constriction.[6,7]

Other CRT techniques which have been employed that avoid CS lead placement include the use of interatrial or interventricular septal puncture for the passage and fixation of an endocardial LV pacing

Table 2 Left ventricular capture and diaphragmatic stimulation thresholds plus pacing impedances during device interrogation at 6-week follow-up visit

Left ventricular capture threshold (V)—at fixed pulse width of 2 ms

	LV-1	LV-2	LV-3	LV-4	RV coil	Can
LV-1		4.5	4.5	4	3.2	2.9
LV-2			6.5	3.5	4	2.4
LV-3		6		7	3	2.6
LV-4		5.5	5		6.5	>7.5

Diaphragmatic stimulation threshold (V)—at fixed pulse width of 2 ms

	LV-1	LV-2	LV-3	LV-4	RV coil	Can
LV-1		1.8	2.6	3.2	3.5	2.9
LV-2			N	N	N	N
LV-3		N		7.5	N	N
LV-4		N	N		N	N

Lead impedance (ohms)

	LV-1	LV-2	LV-3	LV-4	RV coil	Can
LV-1		1047	1001	997	611	684
LV-2			587	854	432	478
LV-3		521		792	380	411
LV-4		884	852		501	494

N = threshold >7.5 V.

lead.[8,9] Transapical puncture techniques for LV endocardial lead fixation have also been employed.[10] These techniques are associated with an increased incidence of arterial thromboembolism due to thrombogenicity of lead components.[11] Leadless endocardial LV pacemaker implantation delivered via a transfemoral arterial access route is in early stages of development and has been associated with vascular access complications, device embolism, and stroke.[12] Use of the LIPV is a potentially attractive alternate technique and is likely to have a favourable safety profile in comparison to the methods described above.

The current literature offers scarce information concerning the anatomy of the LIPV and its potential variations. Clinical interest in techniques for embolization of gastrointestinal varices in subjects with portal hypertension has stimulated some academic interest in the field. An examination of 330 cadaveric subjects revealed that LIPV drainage flowed into the IVC, inferior to the diaphragm, in 37% of subjects[13] (*Figure 7*). A small preceding study of the LIPV in 20 subjects, noted that the vessel origin typically commences from above the diaphragm, adjacent to the apex of the heart.[15] Taking this into account, it is reasonable to assume that the LIPV anatomy provides access to a number of potential locations for LV stimulation in more than one-third of patients.

In our case subject, the LIPV was accessed immediately inferior to the right atrium IVC junction. This allowed uncomplicated cannulation of the vessel with standard CS guide support for delivery of the
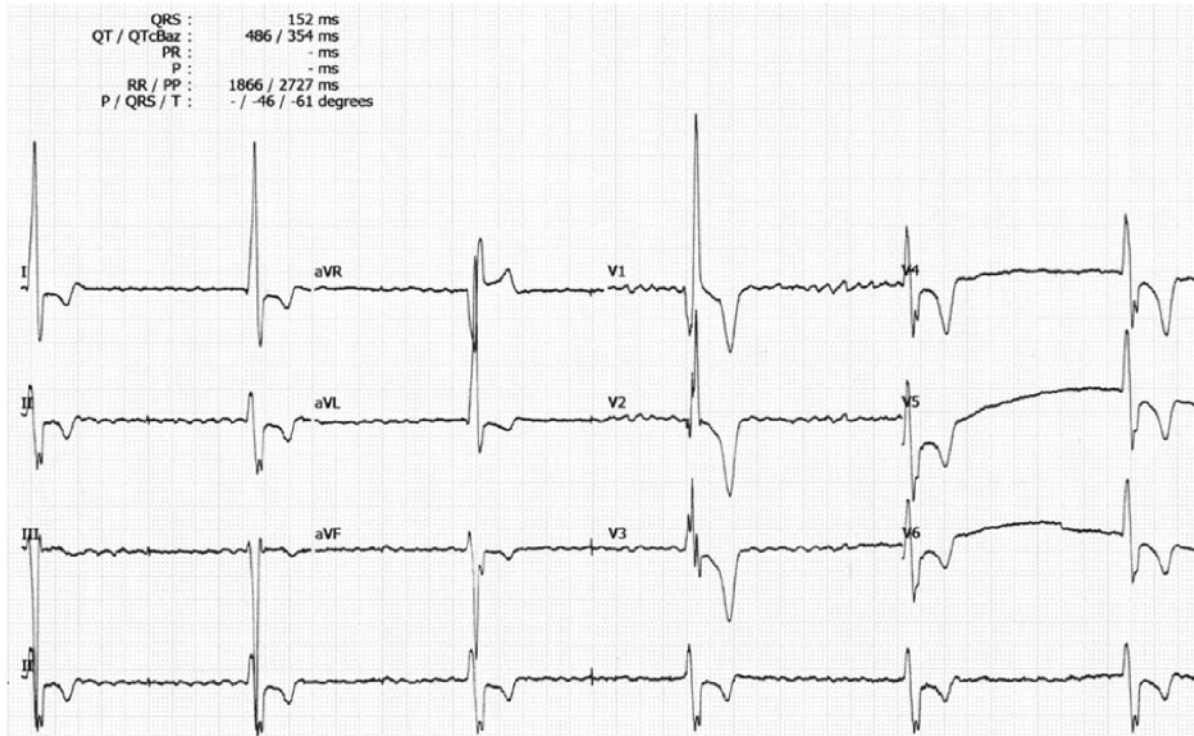
Figure 4 Post-implant electrocardiogram showing underlying native rhythm.
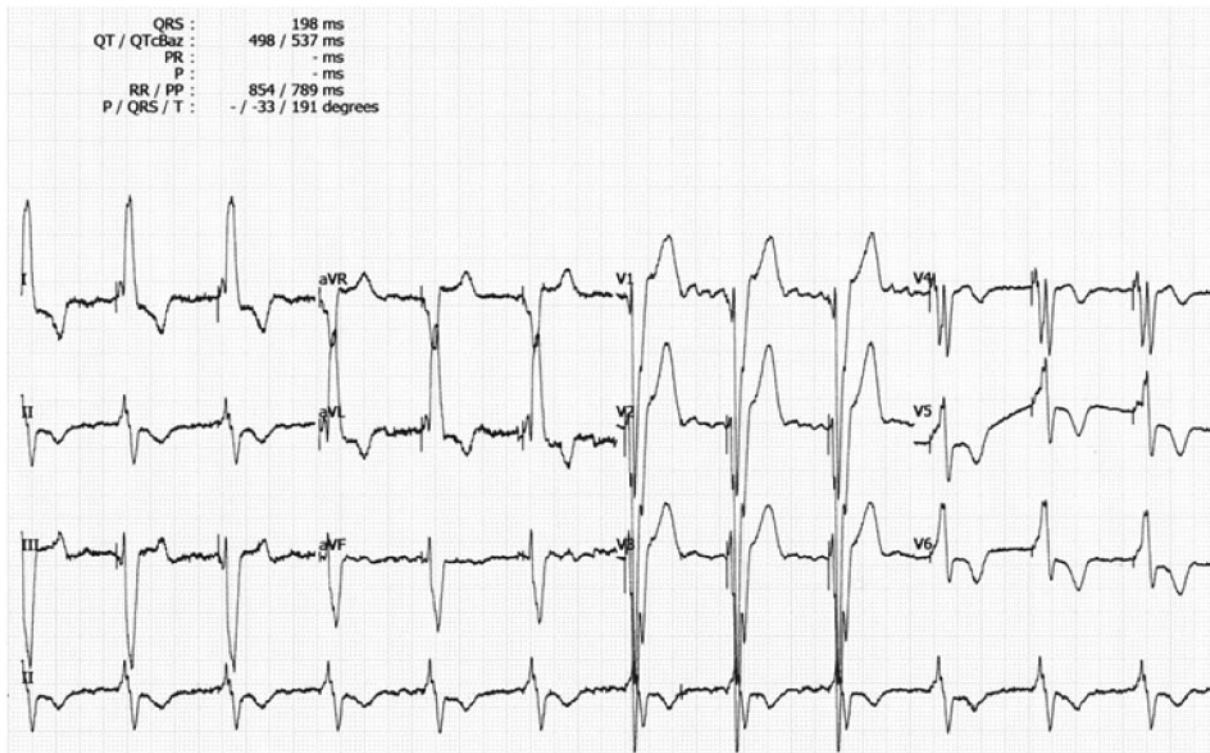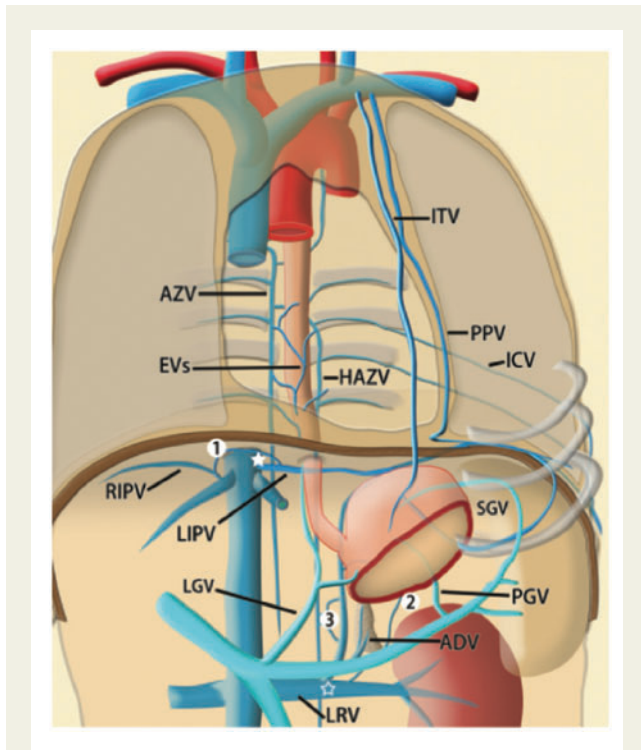
Figure 5 Post-implant electrocardiogram showing right ventricular pacing.

Figure 6 Post-implant electrocardiogram showing biventricular pacing.

Figure 7 The anatomy of the left inferior phrenic vein and surrounding veins of the thorax and abdomen. 1, pre-caval interphrenic anastomotic vein; 2, anastomotic vein to the renal capsular vein and adrenal vein; 3, paravertebral anastomotic veins; ADV, adrenal vein; AZV, azygos vein; EV, oesophageal vein; HAZV, hemiazygos vein; ICV, intercostal vein; ITV, internal thoracic vein; LGV, left gastric vein; LIPV, left inferior phrenic vein; LRV, left renal vein; PGV, posterior gastric vein; PPV, pericardiophrenic vein; RIPV, right inferior phrenic vein; SGV, short gastric vein; ☆, termination of the LIPV into the inferior vena cava (IVC); ★, termination of the LIPV into the left renal vein. Reproduced from Reference 14 with permission from the Radiological Society of America.

LV lead. Fluoroscopy views suggest the distal electrode was positioned adjacent to the posterolateral aspect of the ventricle at the mid-LV level making it an ideal target area.

Stimulation of phrenic nerve is a well-recognized complication of CS lead placement. In the thorax, the nerve runs anterior to the root of the lung traversing the basal region of the anterior interventricular vein, the mid-region of left marginal veins, the apical region of inferior and middle cardiac veins, before reaching the diaphragm.[16] The close association with the coronary venous system may give rise to phrenic nerve capture. Contrary to our expectations, it was possible to identify a number of pacing vectors with LV capture in the absence of diaphragmatic stimulation. The unipolar pacing configurations (LV electrodes 1–4 to can) and more widely spaced bipolar configurations (LV electrodes 1–4 to RV coil) resulted in the least observed diaphragmatic stimulation. Prior observations have suggested that an inverse relationship exists between electrode spacing and phrenic nerve capture thresholds.[17] It may be that the diaphragmatic stimulation, we observed during bipolar pacing between the LV lead electrodes, resulted from local diaphragmatic capture, rather than capture of the phrenic nerve itself. This pattern of behaviour might be expected considering the novel lead location.

Short-term clinical follow-up suggested that CRT delivery through the LIPV had achieved a clinical response with improvement in symptoms and LV function supported by TTE evidence at 10 months. Device interrogation confirmed the lead position to be stable with no deterioration in electrical parameters at both 6 weeks and 22 months following implantation.

Conclusion

During implantation of CRT, lead placement in the LIPV may be a viable alternative to epicardial, transeptal, or transapical lead placement if satisfactory LV pacing cannot be obtained from within the CS or its tributaries. Anatomy potentially suitable for LIPV instrumentation and lead delivery may be present in approximately one-third of individuals.

Lead author biography

Dr Rob McIntosh completed his medical degree in Scotland in 2003. He undertook cardiology subspecialty training in London, based at Imperial College and The Royal Brompton and Harefield NHS Trusts. Prior to being appointed as a consultant in the UK, he spent 2 years completing international fellowships in Wellington, NZ (Complex Cardiac Device Implantation) and Waikato, NZ (Coronary Artery Intervention). Dr McIntosh is based at The Royal Derby Hospital where he leads the Cardiac Devices and Heart Failure services. He also acts for the Derbyshire Interventional Cardiology service, treating both acute and stable patients who have coronary artery disease.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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