

Intensive isotonic training modifies basal and exercise Doppler indexes of systolic function: a comparative study of athletes and sedentary men. *Am J Cardiol* 2001;88:594–598.

9. Perloff D, Grim C, Flack J, Frohlich ED, McDonald M, Morgenstern BZ. Human blood pressure determinations by sphygmomanometry. *Circulation* 1993; 88:2460–2470.

10. Nichols WW, O'Rourke MF, Avolio AP, Yaginuma T, Murgo JP, Pepine CJ, Conti CR. Effects of age on ventricular-vascular coupling. *Am J Cardiol* 1985; 55:1179–1184.

11. Fisman EZ, Ben-Ari E, Pines A, Drory Y, Shiner RJ, Motro M, Kellermann JJ. Pronounced reduction of aortic flow velocity and acceleration during heavy isometric exercise in coronary artery disease. *Am J Cardiol* 1991;68:485–491.

12. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 1978;58:1072–1083.

13. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man. Anatomic validation of the method. *Circulation* 1977;55:613–618.

14. Keul J, Dickhuth HH, Lehmann M. Effect of static and dynamic exercise on

heart volume, contractility, and left ventricular dimensions. *Circ Res* 1981; 48(suppl 1):I-162–I-170.

15. Gardin JM, Davidson DM, Rohan MK, Butman S, Knoll M, Garcia R, Dubria S, Gardin SK, Henry WL. Relationship between age, body size, gender, and blood pressure and Doppler flow measurements in the aorta and pulmonary artery. *Am Heart J* 1987;113:101–109.

16. Mowat DHR, Haites NE, Rawles JM. Aortic blood velocity in healthy adults using a simple ultrasound technique. *Cardiovasc Res* 1983;17:75–80.

17. Ikaheimo MJ, Palatsi J, Takkinen JT. Noninvasive evaluation of the athletic heart: sprinters versus endurance runners. *Am J Cardiol* 1979;44:24–30.

18. Seals DR, Hagberg JM, Spina RJ, Rogers MA, Schechtman KB, Ehsani AA. Enhanced left ventricular performance in endurance trained older men. *Circulation* 1994;89:198–205.

19. Fagard R, Van den Broeke C, Amery A. Left ventricular dynamics during exercise in elite marathon runners. *J Am Coll Cardiol* 1989;14:112–118.

20. Fisman EZ, Frank AG, Ben-Ari E, Kessler G, Pines A, Drory Y, Kellermann JJ. Altered left ventricular volume and ejection fraction responses to supine dynamic exercise in athletes. *J Am Coll Cardiol* 1990;15:582–588.

Safety of Subxyphoid Pericardial Access Using a Blunt-Tip Needle

Arjuna P. Mannam, MD, Kalon K.K. Ho, MD, Donald E. Cultip, MD,
Joseph P. Carrozza, MD, David J. Cohen, MD, Beverly H. Lorell, MD, and
Roger J. Laham, MD

The pericardial space may serve as a potential drug delivery reservoir with sustained myocardial delivery and reduced systemic recirculation of therapeutic agents.^{1–4} “Normal” (without effusion) pericardial access has been achieved by transatrial⁵ or subxyphoid access using the PerDUCER device (CorMedicus Inc, Columbia Heights, Minnesota).⁶ We have recently reported subxyphoid access of the normal pericardium using a blunt-tip needle in animal models for angiogenic drug delivery, demonstrating its safety and efficacy.^{3,7} In addition, although pericardiocentesis is an effective treatment for pericardial effusions, the use of the standard sharp needle, even with echocardiographic guidance,^{8,9} is associated with a low but significant risk of adverse events, including right ventricular puncture and coronary laceration.^{8–10} Thus, the use of the standard sharp needle technique for pericardial access for drug delivery or epicardial access (for ventricular mapping) is not possible in the absence of pericardial fluid. We report a pilot study of the use of subxyphoid pericardial access using a blunt-tip needle in patients with pericardial effusion as a first step to evaluate feasibility for normal pericardial access.

•••

Patients were selected for the study if they had a pericardial effusion and were referred for pericardiocentesis. The study was approved by the institutional review board at the Boston's Beth Israel Deaconess Medical Center. After informed consent was obtained, continuous arterial pressure monitoring was achieved through a femoral or radial arterial cannula. Right-sided cardiac catheterization was performed to measure right atrial, right ventricular, and pulmonary capillary wedge pressure, and cardiac output and index were measured using the Fick oxygen saturation method.

The subxyphoid area was prepped and draped, and a local anesthetic solution (2% lidocaine) was administered to the subxyphoid area. An epidural blunt-tip introducer needle (Tuohy-17) was introduced through the subepigastric region under fluoroscopic guidance with a continuous positive pressure of 20 to 30 mm Hg (achieved by saline infusion using an intraflow system; Figure 1). In addition, an electrocardiographic lead was attached to the needle with continuous electrocardiographic monitoring for ST-segment elevation. Positive pressure was used to push the right ventricle (with a lower pressure) away from the needle's pathway upon pericardial entry, which was suspected after an increase in the saline flow through the intraflow system. Pericardial access was confirmed by the injection of 1 ml of diluted contrast under fluoroscopy (Figure 2).^{3,7} Pericardial pressure was then measured and matched to right atrial pressure to assess for the presence of cardiac tamponade. A soft floppy-tip 0.025-in guidewire was then advanced to the pericardial space and the needle was exchanged for a pericardial drainage catheter with vacuum drainage of the pericardial fluid. Right atrial and pericardial pressure and cardiac index were reassessed at the end of

From the Angiogenesis Research Center and Interventional Cardiology Section, Department of Medicine, Harvard Medical School and Beth Israel Deaconess Medical Center, Boston, Massachusetts. Dr. Laham was supported in part by grants MO1-RR01032 and HL63609 (R.J.L.) from the National Institutes of Health, Bethesda, Maryland. Dr. Laham's address is: Angiogenesis Research Center, Interventional Cardiology Section, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Avenue, Boston, Massachusetts 02215. E-mail: rlaham@bidmc.harvard.edu. Manuscript received July 26, 2001; revised manuscript received and accepted November 29, 2001.

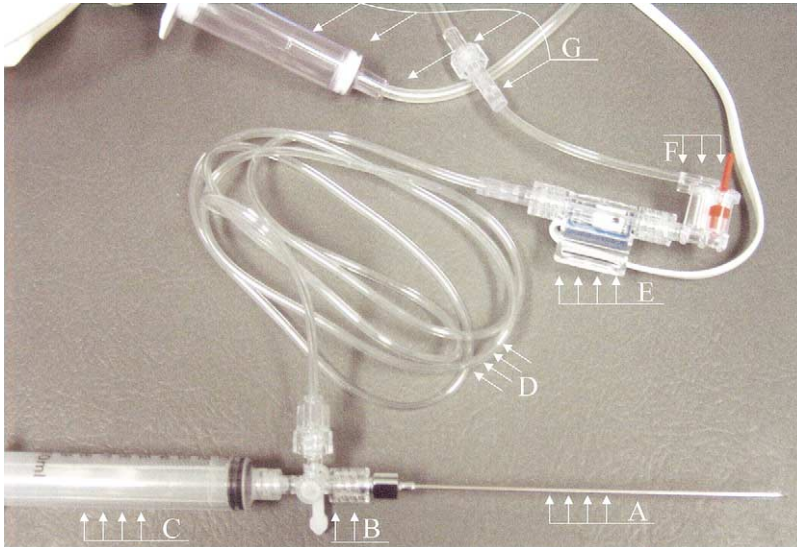


FIGURE 1. Subxyphoid pericardial access setup: a blunt-tip epidural (Tuohy-17) needle (A) is attached to a syringe (C) via a 3-way stopcock (B) hooked through high-pressure tubing (D) to a transducer (E) to monitor pericardial pressure. The system is attached to an intraflow valve (F) hooked to a pressurized saline bag (G). An electrode is also attached to needle for continuous electrocardiographic monitoring (ST-segment elevation).

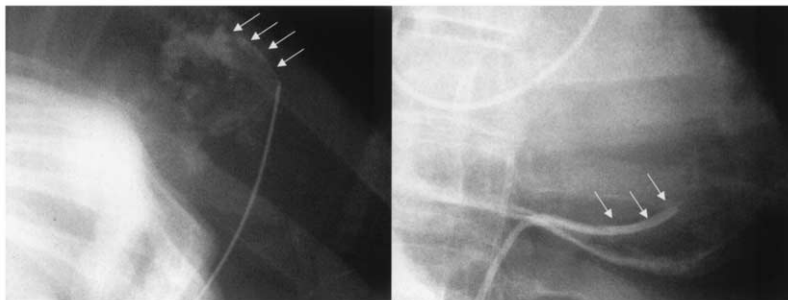


FIGURE 2. Left, subxyphoid access of the pericardial space in a patient with a pericardial effusion. The intrapericardial location of the blunt-tip needle is confirmed by the injection of 1 ml of contrast (arrows) under fluoroscopy. Right, the needle is exchanged for a drainage catheter (arrows) using a 0.025-in soft floppy-tip guidewire.

the procedure and an echocardiogram was performed to confirm pericardial fluid drainage; the drain was left in place for 24 hours with dependent drainage. Echocardiography was repeated at 24 hours to confirm lack of reaccumulation of fluid, after which the drain was removed. The pericardial fluid was analyzed by complete blood count, glucose and protein levels, cytologic examination, and culture.

Follow-up was performed by review of on-line medical records and the patients were contacted at 30 days and 6 months for major adverse events, including death, myocardial infarction, and recurrent pericardial effusion. Data are presented as mean \pm SD. Continuous variables were compared by paired Student's *t* test, and a *p* value ≤ 0.05 was considered statistically significant.

Between September 2000 and March 2001, 12 patients with pericardial effusion requiring drainage were enrolled in the study. Their characteristics and

pressure measurements are listed in Table 1. Mean age was 50 ± 16 years, and 4 were women. Seven patients had a history of malignancy. All patients were symptomatic at the time of presentation; all 12 patients had dyspnea and 7 patients had chest pain. Five patients had a paradoxical pulse >10 mm Hg, 3 patients had hypotension (systolic blood pressure <100 mm Hg), and 5 patients had a low voltage on the electrocardiogram. On echocardiography, 4 patients (33%) had right atrial collapse and 5 patients (42%) had right ventricular collapse. The size of the effusion was 2.1 ± 0.8 cm.

Pericardial access was achieved in all but 1 patient (Table 1), who had a loculated effusion and required surgical drainage after failure of the standard sharp needle technique. No ST-segment elevation was noted during the procedure. Mean right atrial pressure was 16 ± 11 mm Hg, mean pericardial pressure was 16 ± 7 mm Hg, pulmonary capillary wedge pressure was 16 ± 7 mm Hg, and cardiac index was 2.7 ± 0.8 L/min/m² before drainage. After removal of 579 ± 227 ml of pericardial fluid, pericardial pressure decreased to 3 ± 3 mm Hg ($p < 0.05$), right atrial pressure decreased to 10 ± 8 mm Hg ($p < 0.05$), and cardiac index increased to 3.2 ± 0.6 L/min/m² ($p < 0.05$). Postprocedural echocardiography showed resolution of the effusion in the 11 successful pericardiocenteses. There were no procedural complications.

All of the patients had ≥ 6 months of follow-up. One patient (8%) had recurrent pericardial effusion 5 days after the initial procedure and was treated with repeat pericardiocentesis. Three patients (25%) died within 1 month after index pericardiocentesis from their underlying malignancies.

•••

We have reported on the safety, ease of use, and feasibility of pericardial access using a subxyphoid blunt-tip needle approach in patients with pericardial effusion. The use of the combination of a blunt-tip needle, pressurized saline flow, and electrocardiographic (ST-segment elevation) and fluoroscopic guidance has the potential to decrease the procedural complication rate of this technique, possibly making it the procedure of choice for pericardial drainage. Importantly, this technique has the potential to enable access to the normal pericardium using a simple technique, with equipment commonly available in any catheterization laboratory, thus allowing drug delivery

TABLE 1 Baseline Characteristics and Pericardiocentesis Findings

Age (yrs)	Underlying Disease	Drained Fluid (ml)	Pre-Tap			Post-Tap		
			CI (L/min/m ²)	RAP (mm Hg)	PP (mm Hg)	CI (L/min/m ²)	RAP (mm Hg)	PP (mm Hg)
24	Transaminitis	500	2.2	22	14	2.7	6	4
35	Breast adenocarcinoma	800	2.4	14	24	3.2	6	3
37	Aortic aneurysm	1,000	2.0	10	8	2.8	4	1
40	Acute pericarditis	780	2.1	20	22	3.7	16	5
40	Acute myeloid leukemia	400	3.3	13	14	4.2	5	1
48	Pleurisy	300	1.8	24	24	2.6	21	5
50	Non-Hodgkin's lymphoma	400	2.6	3	10	3.2	3	1
54	Renal insufficiency	—	3.8	9	—	—	9	—
54	Non-small-cell lung carcinoma	810	1.9	4	7	2.4	2	1
64	Myeloid dysplastic syndrome	400	2.4	46	26	3.0	26	10
69	Laryngeal carcinoma	500	3.6	14	11	3.3	12	2
80	Melanoma, brain metastases	480	3.9	16	15	4.2	6	1

CI = cardiac index; PP = pericardial pressure; RAP = right atrial pressure.

to the pericardial space and epicardial access for left ventricular mapping.

There are other proposed techniques for pericardial access: the transatrial approach could allow access to the pericardial space via the right atrial appendage.^{5,11} A catheter is used to pierce the right atrial appendage. Pericardial access is then confirmed by placement of a radiopaque guidewire under fluoroscopy.⁵ This technique, however, requires additional skills and may be hazardous in patients with elevated right atrial filling pressure, which is typical of patients requiring pericardial therapy. A second technique utilizes the subxyphoid approach using the PerDUCER device.⁶ A stab incision is made in the subxyphoid area and a 17-gauge angled cannula, with preloaded guidewire, is advanced into the mediastinal space. After cannula removal, a 19Fr sheath and/or dilator is inserted over the wire. The device is positioned over the pericardial cavity and the pericardium is captured by suction and a bleb is formed within a side hole on the PerDUCER tip. A sheathed needle is advanced, puncturing the isolated bleb of the pericardium, allowing pericardial access. The technique we describe offers the advantage of ease of use and utilization of standard cardiac catheterization skills with which most interventional cardiologists are familiar.

We conclude that subxyphoid access of pericardial space can be safely achieved using a novel blunt-tip, pressurized, saline-loaded needle under fluoroscopic and electrocardiographic guidance in

patients with pericardial effusions. A study utilizing this technique in patients with normal pericardium is currently under way.

1. Laham RJ, Simons M, Tofukuji M, Hung D, Sellke FW. Modulation of myocardial perfusion and vascular reactivity by pericardial basic fibroblast growth factor: insight into ischemia-induced reduction in endothelium-dependent vasodilatation. *J Thorac Cardiovasc Surg* 1998;116:1022-1028.
2. Laham RJ, Post M, Sellke FW, Simons M. Therapeutic angiogenesis using local perivascular and pericardial delivery. *Curr Interv Cardiol Rep* 2000;2:213-217.
3. Laham R, Rezaee M, Post M, Novicki D, Sellke F, Pearlman J, Simons M, Hung D. Intrapericardial delivery of fibroblast growth factor-2 induces neovascularization in a porcine model of chronic myocardial ischemia. *J Pharmacol Exp Ther* 2000;292:795-802.
4. Lazarous DF, Shou M, Stuber JA, Dadhanian DM, Thirumurti V, Hodge E, Unger EF. Pharmacodynamics of basic fibroblast growth factor: route of administration determines myocardial and systemic distribution. *Cardiovasc Res* 1997;36:78-85.
5. Waxman S, Pulerwitz TC, Rowe KA, Quist WC, Verrier RL. Preclinical safety testing of percutaneous transatrial access to the normal pericardial space for local cardiac drug delivery and diagnostic sampling. *Catheter Cardiovasc Interv* 2000;49:472-477.
6. March KL, Woody M, Mehdi K, Zipes DP, Brantly M, Trapnell BC. Efficient in vivo catheter-based pericardial gene transfer mediated by adenoviral vectors. *Clin Cardiol* 1999;22:123-29.
7. Laham R, Hung D, Simons M. Subxyphoid access of the normal pericardium: a novel drug delivery technique. *Catheter Cardiovasc Diagn* 1999;47:109-111.
8. Fagan SM, Chan KL. Pericardiocentesis: blind no more! *Chest* 1999;116:275-276.
9. Spodick DH. Intrapericardial therapeutics and diagnostics. *Am J Cardiol* 2000;85:1012-1014.
10. Gibbs CR, Watson RD, Singh SP, Lip GY. Management of pericardial effusion by drainage: a survey of 10 years' experience in a city centre general hospital serving a multiracial population. *Postgrad Med J* 2000;76:809-813.
11. Verrier RL, Waxman S, Lovett EG, Moreno R. Transatrial access to the normal pericardial space: a novel approach for diagnostic sampling, pericardiocentesis, and therapeutic interventions. *Circulation* 1998;98:2331-2333.