

Shining a new light on pericardial fluid

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In a healthy individual, there is 15–50 mL of fluid between the visceral and parietal layers of the fibroelastic pericardium. The normal composition of pericardial fluid is currently ill-defined. In the USA, pericardiocentesis is performed in patients with pericardial disease approximately 1000 times per month.^{1,2} During pericardiocentesis fluid is almost uniformly sent for laboratory analysis per guideline recommendations to quantify general chemistry and cellular composition.³ To date, there is no established methodology to assess pericardial fluid composition nor are there recognised reference values for the normal constituents of pericardial fluid. Interpretation of pericardial fluid composition is commonly performed by extending the Light's criteria validated on pleural fluid analysis to pericardial fluid.^{3,4} The accuracy of this approach to establish if pericardial fluid is transudative or exudative is unknown.

Available data regarding the biochemical and cellular composition of physiological pericardial fluid are sparse. In a study of 30 consecutive patients without pericardial disease undergoing coronary artery bypass grafting or valvular replacement that underwent pericardial fluid analysis, mean fluid lactate dehydrogenase (LDH) was 2.4 times higher and mean protein was 0.6 times lower than serum levels. LDH and protein fluid-serum ratio values of these normal specimens would be classified as exudative per the Light's criteria.⁵ A more recent study performed on 50 patients undergoing cardiac surgery without pericardial disease found that mean fluid LDH levels were 1.1 times higher and total protein in pericardial fluid was 0.5 times lower than plasma levels.⁶ All 50 samples of normal physiological pericardial fluid would be classified by the Light's criteria as exudates. These studies appear to suggest that the composition of pericardial fluid is distinct from pleural fluid and methods for classifying pleural effusions may not apply to pericardial effusions.

In *Heart*, Sabrina Buoro and colleagues sought to define specific reference values

for pericardial fluid analysis.⁷ This study examined a final sample of 120 adult subjects undergoing elective open-heart surgery. The study population was predominantly male (68.1 %) with a median age of 67 years and included those that underwent surgical revascularisation, valve repair/replacement, myectomy and ascending aortic replacement. Subjects with active pericardial disease, heart failure, liver disease, renal disease, recent malignancy, haematological disorders, hypoproteinaemia, pregnancy and diabetes were excluded. At the time of surgery, the pericardial space was opened using an electric scalpel to minimise traumatic bleeding, and two separate 2 mL samples were obtained for analysis. Samples with evidence of haemolysis were discarded. The samples underwent biochemical analyses, automated cell count and optical microscopy.

The authors found that physiological pericardial fluid is rich in protein, albumin, LDH and nucleated cells with low levels of glucose and cholesterol. They derived normal reference values for total protein (1.7–4.6 g/dL), pericardial fluid/serum protein ratio (0.29–0.83), LDH (141–2613 U/L), pericardial fluid/serum LDH ratio (0.40–2.99), albumin (1.19–3.06 g/dL) and pericardium to serum albumin gradient (0.18–2.37 g/dL). Normal reference intervals were also determined by optical microscopy for nucleated cells (278–5608 × 10⁶ cells/L), mesothelial cells (40–3790 × 10⁶ cells/L), leucocytes (19–2210 × 10⁶ cells/L) and lymphocytes (19–1634 × 10⁶ cells/L). While the study's modest sample size likely contributes to wide reference intervals, the results imply normal physiological pericardial fluid would meet traditional criteria for an exudate. The authors hypothesise that the unique composition of pericardial fluid may be due to increased pericardial vasculature permeability, pericardial mechanical stress due to cardiac contractility, or related to the abundant cell types found within the pericardial space.

The findings of the study highlight the potential for diagnostic errors when interpretive tools are used outside of their validated purpose. The Light's criteria were derived on fluid samples from a different physiological space with a composition distinct from pericardial fluid (table 1).

Table 1 Comparison of normal reference intervals of pericardial fluid to transudative pleural fluid

	Pericardial fluid	Pleural fluid transudate
Biochemical components		
Total protein (g/dL)	2.8 (1.7–4.6)	<3.0
Total protein ratio	0.5 (0.29–0.83)	≤0.5
Albumin gradient (g/dL)	1.4 (0.18–2.37)	≥1.2
LDH (U/L)	357 (141–2613)	≤147*
LDH ratio	1.1 (0.40–2.99)	≤0.6
Glucose (mg/dL)	95 (80–134)	65–139†
Total cholesterol (mg/dL)	27 (12–69)	≤45
Cellular counts		
Leucocytes (10 ⁶ cells/L)	503 (35–2210)	125 (83–214)
Mesothelial cells (10 ⁶ cells/L)	1283 (40–3790)	1 (0–2)
Lymphocytes (10 ⁶ cells/L)	304 (19–1634)	23 (16–31)
Polymorphonucleated cells, (10 ⁶ cells/L)	2 (0–116)	1 (0–2)
Macrophages, (10 ⁶ cells/L)	1 (0–207)	75 (64–81)

*Value is two-thirds of the upper limit of normal for those aged 18 years or older (222 IU/L).

†Similar to blood glucose concentration.

Based on the current study, normal physiological samples would be routinely misclassified as exudates due to the rich cellularity and biochemical composition of pericardial fluid. Similar misclassification would likely occur with pathological specimens. More work remains to determine an adequate schema able to differentiate between transudative and exudative pericardial fluid. However, the efforts put forth by the authors to first define the normal composition of pericardial fluid is crucial and should be commended. This study is a step forward in the management of pericardial disease and provides a new standard in interpreting pathological pericardial fluid specimens.

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