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Original article

Pericardial hyperechogenicity and "comets" in patients with acute pericarditis but no pericardial effusion: a comparison study with age-matched healthy controls

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Summary. *Background and aim:* According to the published data and guidelines the diagnosis of pericarditis is mainly clinical; if we exclude patients with pericardial effusion, no single study has been able to relate specific echocardiographic findings to acute pericarditis. We hypothesized that pericardial hyperechogenicity and a defined finding that we named "pericardial comets", in analogy to lung comets, may be associated with acute pericarditis. *Methods:* We retrospectively analysed the echocardiograms of patients aged <50 y/o with a confirmed pericarditis diagnosis and compared them with 2 prospectively healthy controls groups (either < or > 50 y/o) to detect a potential association of pericardial hyperechogenicity and/or pericardial comets with acute pericarditis. *Results:* Comparison between the pericarditis and the control groups did not evidence significant differences regarding the prevalence of hyperechogenicity and pericardial comets when comparing patients with pericarditis and age-matched controls (younger than 50 years); the group of elderly healthy controls (>50 y/o) showed significantly lower prevalence of pericardial hyperechogenicity ($p<0.001$) and comets ($p<0.001$), compared with the other 2 groups. A significantly higher number of patients with pericarditis demonstrated ≥2 pericardial comets compared with age-matched controls (68% vs 48%, $p=0.042$). *Conclusion:* The echocardiographic prevalence of both pericardial hyperechogenicity and comets per patient is heavily influenced by age (inversely proportional), but the presence of at least 2 pericardial comets is significantly more frequent in patients with pericarditis than in healthy aged-matched controls. Nonetheless, this echocardiographic finding may have limited clinical usefulness, due to the frequent detection of ≥2 comets in healthy young subjects also. (www.actabiomedica.it)

Key words: pericarditis, hyperechogenicity, comet artefact, echocardiography

Background

Pericarditis is a condition defined by symptoms and signs of inflammation of the pericardium, caused by a wide spectrum of diseases; still, in a large number of cases a cause is not identified and pericarditis is finally diagnosed as idiopathic (1).

Presently, the epidemiology of pericarditis is uncertain and the overall incidence of acute forms is difficult to establish, since a significant amount of cases probably remains undiagnosed.

According to the published data and current guidelines (1,2) the diagnosis of pericarditis is mainly clinical; if we exclude patients with manifest pericardial effusion, no single study has been able to specifically relate specific echocardiographic findings to acute pericarditis. We hypothesized that pericardial hyperechogenicity and a newly defined echocardiographic

finding that we named "pericardial comets" (in analogy to "lung comets" appearance) (3-6) may be associated with confirmed acute pericarditis. In our experience we have also anecdotally noted higher prevalence of hyperchoic pericardium in young subjects.

We retrospectively analyzed the echocardiograms of patients with a confirmed pericarditis diagnosis and aged less than 50 and compared their data with 2 prospectively collected healthy controls groups (either aged less or more than 50), to detect a potential association of those 2 echocardiographic findings (pericardial hyperechogenicity and pericardial comets) with acute pericarditis and/or with aging.

Methods

Case selection: We retrospectively evaluated all the clinical data (discharge letter, electronic and paper clinical records) of each patient discharged from the Parma University Hospital with a DRG diagnosis of acute pericarditis from January 2009 to December 2011. To confirm the accuracy of the discharge diagnosis, according to current guidelines and published diagnostic criteria (1,2), four criteria were considered: 1) chest pain (typical or atypical for pericarditis), 2) presence of pericardial friction rub, 3) presence of widespread concave ST-segment elevation; 4) presence of pericardial effusion. A diagnosis of pericarditis was confirmed in our study, similarly to what is proposed by Imazio et al (2), when at least 2 of those four proposed criteria were fulfilled in the same subject.

All patients with a confirmed pericarditis diagnosis according to the abovementioned definition were initially selected for our study and the following exclusion criteria then applied: 1) echocardiogram not performed during the index hospitalization or only partial availability of echocardiographic images for offline evaluation; 2) presence of pericardial effusion at echocardiogram; 3) unavailability of full clinical documentation; 4) age <18 y/o or > 50 y/o, 5) history of a prior episode of pericarditis.

Controls selection: Controls were prospectively enrolled among hospital workers and then divided, as per protocol, into 2 separate control groups based on age < or > 50 y/o.

Criteria for selecting controls were the following: 1) Asymptomatic and apparently healthy volunteers (hospital workers and medical fellows), 2) without known cardiac illness or chest pain history and 3) with a final diagnosis of a completely normal echocardiogram.

Echocardiography: Echocardiographic examinations of cases/controls satisfying all enrollment criteria were reviewed from our digital archive and parasternal long-axis views were specifically analyzed for the presence of pericardial hyperechogenicity and presence/number of pericardial comets (Figure 1 and 2). All studies were performed in our lab with Philips ie33 equipped with standard S5 probe and, according to our lab procedure, routinely using the "iScan" signal equalization button before acquiring each cardiac clip; this minimizes the possibility that received signals exceed the dynamic range of the machine. Hyperechogenicity of the pericardium was defined as markedly elevated echoic signal of the pericardium compared to surrounding structures, quantified with offline sampling (Philips QLab 6.0 software) as a posterior pericardial signal intensity (dB) empirically defined at least double compared with the adjacent myocardium intensity

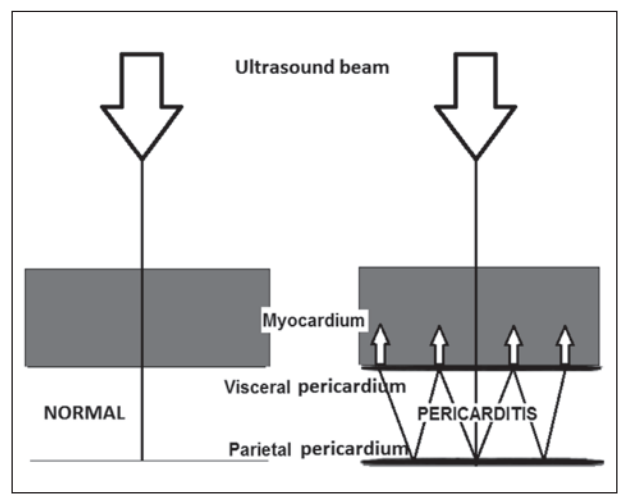

Figure 1. The hypothesized physical and anatomic basis of echocardiographic pericardial comets/artifacts. Left: normal healthy subject. Right: Reflections of the ultrasound beam by the thickened visceral/parietal pericardium creates "comet-tail" artifact reflected from the extravascular pericardial water in patients with pericarditis, and then received by the ultrasound probe

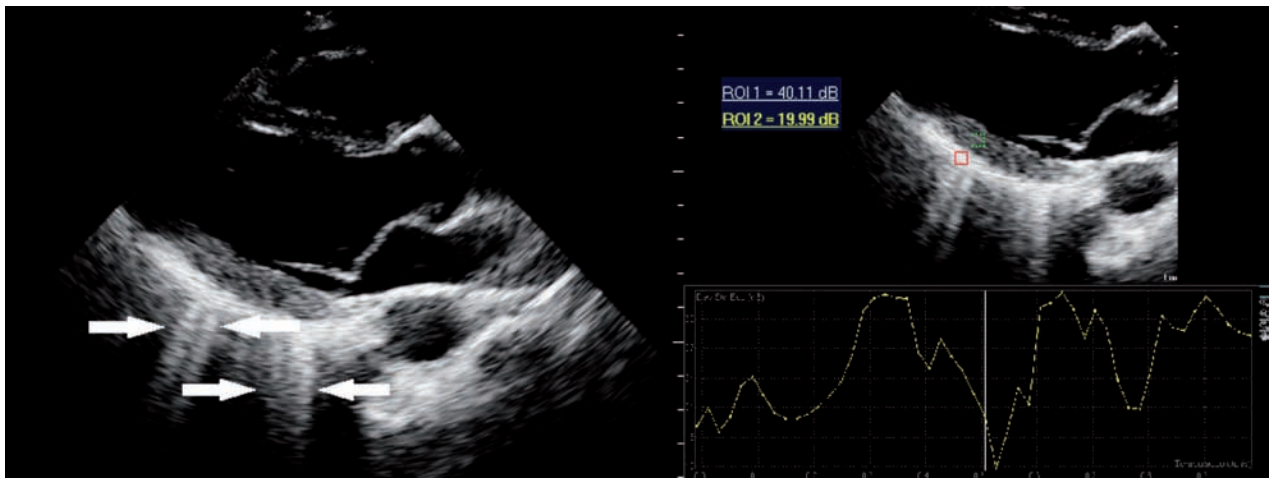

Figure 2. Patient with confirmed acute pericarditis and no pericardial effusion. On the left, the 2 pericardial comets are delimited by convergent arrows. On the right, the visually apparent pericardial hyperechogenicity is confirmed by quantification of the pericardium signal intensity which is slightly more than double (40.11dB) compared with the adjacent myocardium (19.99 dB)

(see figure 2 showing a borderline case, right); pericardial comets were defined as echogenic wedge-shaped signals with narrow origin from the pericardium[10], of at least 1 cm width, often composed by a couple of grouped parallel vertical lines and they were counted using the frame in which the identifiable number was highest (see figure 2, left). All echocardiograms were randomly and blindly evaluated for these characteristics by an expert operator (N.G.) unaware of patient clinical allocation in either confirmed pericarditis or control groups. Intraobserver repeatability for pericardial/myocardium ratio was also calculated in 10 parasternal long-axis clips. Mean and standard deviation was used to describe continuous data. Differences between groups were compared using the t-test for unpaired data or the chi-squared test, as appropriate for each type of variable.

Results

Of the initial 158 patients discharged with a DRG diagnosis of acute pericarditis from our hospital during the study time period, 13 were excluded because satisfying <2 criteria among the 4 chosen in our study definition of pericarditis, 2 because of unavailable clinical documentation, 18 because of unavailable or incomplete echocardiographic study during the index hospitalization, 37 because of the presence of pericardial effusion and 38 because aged >50 y/o.

Patients finally enrolled in the pericarditis group were 50; consequently, the same number of first consecutive 50 subjects <50 y/o and first consecutive 50 subjects >50 y/o satisfying selection criteria for controls were chosen and their echocardiograms analysed similarly to cases. Baseline characteristics of patients in the pericarditis group are shown in table 1.

In the pericarditis group, 100% of patients satisfied at least 2/4 of the study criteria for confirmed pericarditis, while 24% satisfied 3/4 criteria and no single patient presented all 4/4 criteria, which is easily explained by pericardial effusion (1 of the 4 diagnostic criteria) representing also an exclusion criterion. Although laboratory findings were not considered among the 4 criteria used to diagnose pericarditis, in the pericarditis group 52% of patients had elevation of serum CK-MB and 68% of serum troponin I above the upper limit of normal.

In the pericarditis group, off-line evaluation of echocardiographic images by an expert operator showed the presence of pericardium hyperechogenicity, according to quantitative analysis, in 44/50 patients (88%) and an overall number of comets of 77, with a mean comet number per patient of 1.54±1.5.

The echocardiograms of the control groups, similarly assessed for the presence of pericardium hyper-

Table 1. Pericarditis group

Variable	n=50
Mean Age y/o (±SD)	33.7 (8.4)
Male Gender n (%)	38 (76)
Pericarditic Chest Pain n (%)	50 (100)
Pericardial Rub n (%)	4 (8)
Diagnostic ECG Changes n (%)	48 (96)
Fulfilled Diagnostic Criteria (2/4) for Pericarditis n (%)	50 (100)
Fulfilled Diagnostic Criteria (3/4) for Pericarditis n (%)	12 (24)
Fulfilled Diagnostic Criteria (4/4) for Pericarditis n (%)	0 (0)
Known Autoimmune Disease n (%)	0 (0)
Tubercolosis n (%)	0 (0)
Arrhytmias n (%)	4 (8)
Increased Ck-Mb n (%)	26 (52)
Increased Troponin I n (%)	34 (68)
Fever/Infection within prior 2 Weeks n (%)	43 (86)
Increased CRP Value n (%)	43 (86)

echogenicity and comets, showed the following results: in the group of control subjects younger than 50, pericardial hyperechogenicity was evidenced in 44 out of 50 patients (88%) with overall 80 comets, and a mean comet number per patient of 1.6±1.97; in the group of controls older than 50, hyperechogenicity was detected in 27 out of 50 patients (54%) and the overall number of comets was 22, for a mean comet number per patient of 0.44± 0.84 (see table 2).

Comparison between the pericarditis group of patients and the two control groups did not evidence significant differences regarding the prevalence of hyperechogenicity and pericardial comets when comparing patients affected by pericarditis and age-matched controls (younger than 50 years); on the contrary, the group of controls older than 50 y/o showed a statistically significant lower prevalence of pericardial hyperechogenicity ($p<0.001$) and comets ($p<0.001$), compared with the other 2 groups (table 2). A statistically significant higher number of patients with pericarditis demonstrated ≥2 pericardial comets compared with age-matched (<50 y/o) controls (68% vs 48%, $p=0.042$).

Discussion

Until now, no study had systematically evaluated the relationship between an echocardiographic findings anecdotally related to pericarditis, such as hyperechogenicity of the pericardium, and their true incidence in patients with an established diagnosis of pericarditis based on standardized and rigorous clinical criteria.

We also decided to analyse the potential association of "pericardial comets" with pericarditis, since in our clinical practice we frequently noticed these echocardiographic finding in patients referred for suspected pericarditis, somewhat similarly to the lung comets already known to be related to pulmonary oedema/ extravascular lung water.

The main finding of this study is that in fact both pericardial hyperechogenicity and pericardial comets are inversely proportional to and mainly driven by age more than by the presence of pericarditis, with younger control subjects or patients with pericarditis (all aged <50 y/o) *indifferently* more prone to show both echocardiographic signs when compared with older

Table 2. Comparison among groups

Variable	Group 1 Pericarditis Age <50	Group 1 vs 2	Group 2 Controls Age<50	Group 2 vs 3	Group 3 Controls Age >50	Group 1 vs 3
Patient number	50	------	50	------	50	-----
Age (mean±D)	33.7±8,4	p=0.27	31.8±8.6		72.2±10.8	
Male gender n (%)	38 (76)	p=0.086	30 (60)	p=0.68	32 (64)	p=0.19
Comets number per patient (mean±SD)	1.54±1,5	p=0.86	1.6±1.97	p<0.001	0.44±0.84	p<0.001
Subjects with at least 2 comets n (%)	34 (68)	p=0.042	24 (48)	p=0.023	13	p<0.0001
Pericardial Hyperechogenicity n (%)	44 (88)	p>0.99	44 (88)	p<0.001	27 (54)	p<0.001

healthy subjects. Still, there was a slightly but statistically significant higher number of patients with pericarditis who demonstrated ≥2 pericardial comets compared with controls of the same age category (young adults <50 y/o): this association represents an interesting proof of concept, which confirms that pericardial inflammation may truly increases the number of pericardial comets, though this finding remains clinically of little use, because comets (and hyperechogenicity) appear to be also very common in young and *healthy* adults without pericarditis (age matched controls).

To define hyperechogenicity we decided to use a more objective method than visual assessment, not to expose our study to the criticism of being based only on subjective visual evaluation; we measured signal intensity with commercially available quantification software, by sampling the posterior pericardium and adjacent myocardium to measure signal intensity in decibels. We defined hyperechogenicity using > x2 signal intensity cut-off compared with myocardium, using this sharp multiple number for the sake of simplicity, although this cut-off turned out to be rather restrictive (in other words the reader would have visually called pericardial hyperechogenicity more often than the quantitative evaluation indicated) and may have excluded milder forms of hyperechogenicity.

Study limitations

The current study considered a group of "only" 50 patients with confirmed acute pericarditis, due to the restrictive definition used for acute pericarditis (more restrictive than selecting patients based only on their DRG diagnosis code), due to the several exclusion criteria and per-protocol required availability of full echo data and clinical documentation. We preferred to somewhat downsize the cases group (and consequently the control groups to maintain 1:1 ratio) rather than include patients with unconfirmed or vague diagnosis of acute pericarditis. More studies, hopefully including a higher number of subjects, may be required to confirm the neutral/negative findings of the present study.

Conclusions

The echocardiographic prevalence of both pericardial hyperechogenicity and comets is heavily influenced by age (inversely proportional), but the presence of at least 2 pericardial comets is statistically more frequent in patients with pericarditis than in healthy aged-matched controls. Nonetheless, this echocardiographic finding may have limited diagnostic yield and clinical usefulness, due to the frequent detection of ≥2 comets in healthy young subjects also.

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