

Hyperuricemia Destroying the Heart: Are Tophaceous Valves that Rare?

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Abstract

While the extraarticular deposition of urate crystals and its general cardiovascular impact are well recognized, the specific association between hyperuricemia and heart valve disease remains under-documented. Currently, only isolated cases of tophaceous valves have been reported, highlighting a significant gap in the literature. This narrative review aims to investigate the available data on monosodium urate (MSU) deposition on heart valves, assessing its prevalence, detection via advanced imaging modalities, and potential contribution to structural valve dysfunction. A literature search was conducted in the PubMed (MEDLINE) database for records published up to April 2026. The search strategy utilized Boolean operators to combine terms for specific heart valves with “gout,” “urate crystals,” “tophi,” and imaging modalities relevant to extraarticular gout. Relevant case reports, imaging studies, and primary references were curated and analyzed. The search identified 10 historical case reports and one systematic review detailing histologically proven tophaceous valves,

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predominantly affecting the mitral and aortic valves. Historically, valvular tophi were considered exceedingly rare, often manifesting as incidental postmortem or postoperative findings. However, recent data utilizing Dual-Energy Computed Tomography (DECT) contrasts this paradigm. A prominent DECT study revealed cardiovascular MSU deposition in 86.4% of gout patients, with 18.2% specifically exhibiting urate deposits within the heart valves. These imaging findings were histologically validated, demonstrating DECT's accuracy in differentiating MSU from typical degenerative calcinosis, which may macroscopically mask urate deposits during routine histopathological examinations. Although isolated case reports suggest valvular tophi are rare, advanced imaging reveals a significantly higher prevalence of MSU deposits in cardiac valves. This discrepancy highlights the necessity for increased clinical vigilance regarding valvular involvement in hyperuricemic individuals and warrants further investigation into its precise role in structural heart disease.

Keywords: gout, hyperuricemia, heart valves, extraarticular urate deposits, tophaceous valve, X-Ray computed tomography

1. Introduction

Gout is one of the most common metabolic diseases of our times [1-3] and the extraarticular effects of hyperuricemia and especially its contribution to the cardiovascular risk are well recognized [4-6]. Even though treating isolated hyperuricemia even in the absence of other cardiovascular risk is not recommended [5, 7], there is an ongoing debate as data accrues on even isolated hyperuricemia leading to both articular and extraarticular deposition of precipitated crystals of monosodium urate (MSU) [8]. Especially in untreated or poorly managed gout MSU deposition takes form of gouty tophi with well-known typical histological structure [9]. Apart from the joints and their surrounding tissues, tophi have been found in different loci in head and neck, around nerves, in the axial skeleton etc. [10]. Over time, tophi can lead to erosion of the articular cartilage and periarticular fibrosis of the surrounding soft tissues [11, 12]; similar changes have been found in kidney, nerves and vessels [13, 14]. However, data on particular association of gout or hyperuricemia with heart valve disease seem to be insufficient. Only a few cases of tophaceous valves can be found in the literature [13].

In this review we aim to investigate further the data available on MSU deposition on heart valves specifically both by case reports and imaging modalities, its prevalence as well as its contribution on valve dysfunction.

Throughout this review, we distinguish between histologically confirmed tophi, as reported in the case-report literature, and imaging-detected urate deposits, as identified by DECT, recognizing that these represent related but non-equivalent findings.

2. Search Methodology and Results

To construct this biomedical review, we employed a systematic methodology adapted from the framework proposed by Gasparyan et al. [16]. A literature search was executed across the PubMed (MEDLINE) database, covering all available records up to April 2026 in two directions – capturing case reports on tophaceous heart valves on the one hand, and looking up the relevant imaging modality for visualizing those. Furthermore, the discussion incorporates insights derived from primary references, auxiliary database searches, and the authors' clinical expertise and professional judgment [16].

2.1. Case Reports

Our search strategy utilized Boolean operators to combine the terms “valve,” “mitral valve,” “aortic valve,” and “tricuspid valve” with (AND) “gout,” “urate crystals,” and “tophi.” The initial inquiry yielded 399 records. Following the removal of duplicates, review papers, and non-pertinent entries, the primary data were curated and are detailed in the subsequent section.

As a result of our search, 10 case reports of tophaceous valves—predominantly histologically confirmed—were identified, along with one 2019 review summarizing eight of these cases [15, 17-26]. Table 1 summarizes the demographic, clinical, and diagnostic characteristics of these 10 cases, together with the reviewing authors' judgment on whether the valvular tophus was likely to have contributed causally to valve dysfunction or represented an incidental, non-causal finding. The earliest published report in the medical literature is attributed to Coupland (referenced by Bunim and McEwen [18]) and dates back to 1873. The author described “tophi in a calcified aortic valve based on a positive murexide test, [which] merely represented incidental urate deposition in an old calcareous deposit” [18].

In 1940, Bunim and McEwen reported a patient with clinically diagnosed chronic tophaceous gout who lacked any evidence of cardiac disease. However, postmortem histological analysis revealed a typical tophus on the posterior mitral leaflet, composed primarily of urates and cholesterol. In

1982, Dennstedt and Weilbaecher reported another incidental finding of a gouty tophus in a surgically excised mitral valve. Histological examination showed birefringent, dichroic crystals consistent with uric acid [19].

The first case linking chronic tophaceous gout to the aortic valve was reported in Australia in 1983 by Jaworski and Gibson. An autopsy revealed tophi on the aortic valve leaflets containing birefringent, dichroic uric acid crystals [20]. That same year, Curtiss et al. described a 31-year-old man with congenital heart disease (Taussig-Bing anomaly) and tophaceous gouty arthritis [21]. The patient was treated for suspected infective endocarditis due to clinical signs of a brain abscess and a newly developed regurgitant heart murmur. An autopsy revealed that the valvular dysfunction was caused by sterile tophi located along the coaptation line of the pulmonary valve, with similar deposits noted on the mitral valve.

In 1984, Scalapino et al. presented the case of a 68-year-old woman with chronic tophaceous gout, a history of rheumatic heart disease, and signs of heart failure. Echocardiography revealed thickened, immobile mitral leaflets and a dilated left atrium containing a dense thrombus [22]. Surgical intervention included two aortocoronary bypasses, mitral valve replacement, and the removal of the atrial thrombus. The authors concluded that subannular tophi prevented proper leaflet opening and contributed to leaflet rigidity.

The majority of these cases were summarized in a 2019 systematic review by LaMoreaux and Chandrasekaran [13]. In their review, the average patient age was 60.9 years, with a strong male predominance (89%). The mitral valve was most frequently affected, followed by the aortic and pulmonary valves; notably, no tricuspid valve involvement was reported. Diagnosis across these cases was typically established through histopathological examination.

Table 1. Summary of the 10 historical case reports of histologically or clinically identified tophaceous heart valves.

#	Author, Year [Ref]	Age/ Sex	Valves Affected	Clinical Presentation	Diagnostic Confirmation	Clinician's Judgment on Causality
1	Coupland, 1873 [17]	NR	Aortic	Incidental finding on a calcified aortic valve	Murexide test	Incidental - original author described it as “merely...incidental urate deposition in an old

						calcareous deposit"
2	Bunim & McEwen, 1940 [18]	NR	Mitral (posterior leaflet)	Clinically diagnosed chronic tophaceous gout; no clinical evidence of cardiac disease during life	Postmortem histology (urate + cholesterol)	Incidental - postmortem finding with no antemortem cardiac disease
3	Dennstedt & Weilbaecher, 1982 [19]	NR	Mitral	Found in a surgically excised mitral valve	Histology / polarized light (birefringent, dichroic crystals)	Incidental - explicitly reported as an incidental finding
4	Jaworski & Gibson, 1983 [20]	NR (adult)	Aortic	Chronic tophaceous gout; aortic valve stenosis found at autopsy	Postmortem histology (birefringent, dichroic crystals)	Not explicitly stated - tophi and stenosis co-existed; authors did not assert causation
5	Curtiss et al., 1983 [21]	31y, M	Pulmonary (primary); mitral (also involved)	Congenital heart disease (Taussig-Bing anomaly); new regurgitant murmur and brain abscess, suspected endocarditis	Autopsy/histology (sterile tophi)	Causal - authors stated dysfunction "was caused by" the tophi
6	Scalapino et al., 1984 [22]	68y, F	Mitral	Chronic tophaceous gout, rheumatic heart disease history, heart failure, mitral stenosis, LA thrombus	Echocardiography + surgical histology (MVR specimen)	Causal - subannular tophi held to prevent leaflet opening/cause rigidity
7	Gawoski et al., 1985 [23]	Elderly, M	Aortic	Long-standing gout; valve surgically resected (calcified)	Histology + X-ray diffraction (confirmed MSU + hydroxyapatite/whitlockite)	Incidental - tophus found alongside dystrophic calcification, the presumed primary pathology
8	Iacobellis &	NR	Mitral	Asymptomatic cardiac finding;	NR (full text not accessible)	Incidental - title reports it as "rare

	Iacobellis, 2004 [24]			severe gouty tophaceous arthritis elsewhere		and asymptomatic”
9	Koffi et al., 2010 [25]	NR	NR	NR (full text paywalled)	NR	NR
10	Rohani et al., 2012 [26]	75y, M	Mitral (posterior leaflet)	10 yr history of tophaceous gout, acute flare; incidental echo finding during HF screening	Echocardiography only (TTE+TEE) - not histologically confirmed	Incidental - authors state “without significant valve dysfunction”; diagnosis was presumptive

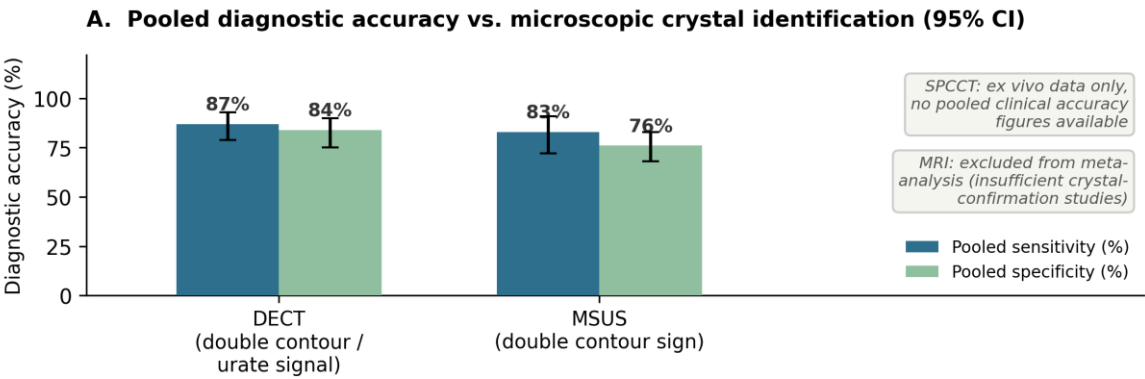
Abbreviations: NR: not reported / not available in the accessible source. MVR: mitral valve replacement; MSU: monosodium urate; TTE: transthoracic echocardiography; TEE: transesophageal echocardiography; HF: heart failure; LA: left atrium.

2.2. Imaging Modalities for Detecting MSU Deposits in the Heart Valves

A structured literature search was conducted to evaluate imaging modalities relevant to extraarticular monosodium urate (MSU) deposits. The primary search utilized the exact Boolean string: ("extraarticular gout" AND "imaging"). Additional scoping queries were executed using the search strings ("MSU deposits" OR "tophi" OR "heart valves" OR "tophaceous valves") AND "imaging".

Articles were filtered based on their direct relevance to the imaging of extraarticular MSU deposition. The primary search string yielded 35 records that met this inclusion criterion. Upon abstract review, it was noted that none of these initial 35 records directly addressed deposition within the heart valves. However, subsequent citation tracking of this literature cohort identified a recurrent and highly relevant article [27]. This specific study, which compared Dual-Energy Computed Tomography (DECT) with histopathology, explicitly described valve crystal deposition and was subsequently included in the review.

2.2.1. Imaging Modalities for the Detection of Extra-Musculoskeletal Monosodium Urate Deposits



B. Comparative features of imaging modalities for extra-articular / valvular MSU deposits

	DECT	MSUS	SPCCT	MRI	Conventional CT
Detects heart-valve MSU deposits (published evidence)	✓	✗	✗	✗	✗
Differentiates MSU from calcification	✓	~	✓	✗	~
Radiation-free	✗	✓	✗	✓	✗
Current clinical availability	✓	✓	✗	~	✓

✓ established / yes ~ partial or indirect ✗ not established / no

Figure 1. Comparison of imaging modalities for detecting extra-articular and valvular monosodium urate (MSU) deposits. (A) Pooled sensitivity and specificity of DECT and MSUS against microscopic crystal identification, with 95% confidence intervals [29]; SPCCT accuracy has only been reported in ex vivo studies, and MRI was excluded from the pooled meta-analysis due to insufficient crystal-confirmation studies. (B) Comparative features of the five modalities discussed in the text, based on the evidence summarized above.

Dual-Energy CT (DECT) is currently the most robustly investigated modality for detecting both intra- and extra-articular MSU deposits [28]. The technique exploits the differential X-ray attenuation of MSU crystals at varying energy levels to generate color-coded maps of crystal deposition. When compared to microscopic crystal identification, DECT demonstrates a pooled sensitivity of 87% (95% CI 0.79-0.93) and a specificity of 84% (95% CI 0.75-0.90) [29]. In the context of extra-musculoskeletal applications, DECT has been successfully utilized to visualize MSU deposits in cardiovascular structures, as well as in deep soft tissues, tendons, and bursae [28]. The technology has evolved significantly; third-generation scanners offer improved spectral separation, resulting in fewer equivocal interpretations (a reduction from 33% in 2013 to 16% in 2019) [30].

Musculoskeletal Ultrasound (MSUS) identifies MSU deposits through characteristic features such as the double contour sign (a hyperechoic band overlying the cartilage), soft tissue tophi, and microaggregates [31]. The double contour sign exhibits a pooled sensitivity of 83% (95% CI 0.72-0.91) and a specificity of 76% (95% CI 0.68-0.83) [29]. Although ultrasound is a widely accessible, cost-effective, and radiation-free modality highly valuable for periarticular soft tissues, its utility for extra-musculoskeletal applications is limited. It is highly operator-dependent and lacks the physical capability to evaluate deep internal structures or provide a whole-body assessment of the crystal burden. [28] Nevertheless, recent advancements, including superb microvascular imaging and AI-based deep learning algorithms, continue to enhance its diagnostic accuracy [32].

Multi-energy spectral photon-counting CT (SPCCT) is an advanced technology that uses energy-resolving photon-counting detectors, providing superior spectral separation compared to conventional systems [33]. In ex vivo studies, SPCCT has demonstrated the ability to detect MSU deposits with significantly finer detail than standard DECT [34]. It can also differentiate between distinct crystal types based on their elemental composition, successfully distinguishing MSU from calcium pyrophosphate (CPP) and hydroxyapatite (HA) within calcified tissues [34]. Despite its potential for detailed whole-body crystal assessment, SPCCT remains primarily a research tool with limited clinical availability [33, 34].

Magnetic Resonance Imaging (MRI) effectively visualizes soft tissue abnormalities, tophi, synovial inflammation, and bone marrow edema; however, its images are nonspecific for MSU crystals [35, 36]. On both T1- and T2-weighted sequences, tophi typically present with low to intermediate signal intensity that may also be feature of variety of other pathological structures [37]. Contrast enhancement also lacks diagnostic specificity for gout [37]. Due to an insufficient number of studies utilizing microscopic crystal confirmation (the gold standard), MRI was excluded from the meta-analysis on diagnostic accuracy conducted by Ogdie et al [29].

Conventional CT is capable of visualizing tophi as soft tissue masses with a density of approximately 160 Hounsfield units (HU), thus yielding a relative degree of specificity for MSU [36]. However, its primary limitation is that it cannot reliably differentiate MSU deposits from other crystal types or calcifications in extra-musculoskeletal tissues [35, 37].

2.2.2. Emerging Technologies

The application of deep learning reconstruction techniques to DECT shows significant promise. These algorithms enhance the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR), improving MSU detection while potentially allowing for a reduction in patient radiation exposure [38].

As mentioned above, the only study dealing with MSU deposits in valves is the one by Klauser et al. [27]. The team conducted a prospective case-control study aiming “to compare coronary calcium score and cardiovascular MSU deposits detected by DECT”. Among the 157 participants, 110 had gout (according to the 2015 ACR/EULAR criteria) and the remaining 47 were age- and sex-matched controls. The imaging protocol featured a cardiovascular-optimized software with a density threshold of 150 Hounsfield units aiming to minimize artifacts from tissue calcifications. There was a significantly higher prevalence of cardiovascular MSU deposition in the gout group (86.4%) compared to only 14.9% of the controls. Apart from deposits in the aorta (77.3%) and coronary arteries (33.6%), DECT specifically identified urate deposits within the heart valves - the mitral and tricuspid valves - in 18.2% of the studied group. Analysis of 10 cadavers that displayed positive DECT signals was also performed with histological examination including polarized light microscopy and confirmed the presence of negatively birefringent, needle-shaped MSU crystals in 70% of the cases. Thus, a main conclusion of the study was that DECT accurately discriminates MSU (urate) deposits from calcium in valvular and vascular structures. The authors acknowledge several limitations of their work: its cross-sectional design, the relatively small control group, along with technical challenges such as calcifications masking smaller neighboring urate deposits due to strong signal.

4. Discussion

4.1. Strengths and Limitations

In this narrative review, we aimed to present data available in the scientific literature concerning MSU deposits on cardiac valves. Although the isolated case reports from the last century would suggest that valve involvement is exceedingly rare, the sole study using imaging modality reveals quite a contrasting picture. This is the main limitation of this review and, in fact, of the data available - its scarcity, relying on a single database: a limited number of cases and only one, even though well-designed, case-control study. The second limitation of the data compared is that the case reports presented refer to tophi, while the DECT study discriminated urate deposits

only. This distinction is not merely semantic: a histologically confirmed tophus reflects an organized, chronic deposit accompanied by a characteristic granulomatous tissue reaction, whereas DECT identifies the presence of urate crystals based on their dual-energy attenuation profile alone, without providing direct information on the surrounding tissue response or the maturity of the deposit. Accordingly, DECT-detected valvular urate deposits and histologically confirmed tophaceous valves should be regarded as related but non-equivalent findings, and the higher prevalence reported by DECT cannot be directly equated with a comparable prevalence of true tophi. Notably, although our literature search extended through April 2026, no additional independent imaging studies were identified that replicated or disputed the findings of Klauser et al.; the DECT-based prevalence estimates therefore remain unconfirmed by any second dataset.

Despite these limitations, this review offers several strengths. To our knowledge, it is the first work to systematically juxtapose the historical case-report literature on tophaceous heart valves with the emerging imaging-based evidence on valvular urate deposition, applying a structured search methodology adapted from established narrative-review guidance. By compiling the demographic, clinical, and diagnostic characteristics of all 10 published case reports (Table 1) alongside a critical appraisal of the available imaging modalities (Figure 1), this review provides a practical reference for clinicians and a clear framework for future investigation, while explicitly flagging the non-equivalence between imaging-detected and histologically confirmed findings discussed above.

4.2. Clinical Implications and Future Directions

However, the data presented still suggest that routine postoperative histopathological examinations may frequently fail to identify MSU deposits as the macroscopic appearance of the valve may resemble a typical degenerative calcinosis and thus easily be overlooked. The discrepancy suggests that closer scrutiny of structural valve damage is warranted, particularly in patients with hyperuricemia.

The precise degree to which valvular tophi contribute to structural - and consequently functional - valvular damage remains unclear. In several of the previously discussed reports, tophi were documented as incidental findings, whereas other authors explicitly argued for a causal relationship. Given the current evidence base, this causal relationship should be regarded as unproven, and prospective studies with systematic histological and functional assessment are needed before valvular tophi can be

considered a definitive contributor to structural heart disease. Further studies are required to systematically classify the sites of deposition, investigate the underlying tissue alterations, and account for the impact of concomitant comorbidities.

It is well established that hyperuricemia (serum urate ≥ 6.8 mg/dL) is independently linked to hypertension, chronic kidney disease (CKD), metabolic syndrome, diabetes, and cardiovascular disease [5, 39, 40] via inflammasome activation, oxidative stress, endothelial dysfunction, and reduced nitric oxide bioavailability [40, 41]. Furthermore, epidemiological studies have shown that elevated uric acid levels are predictive of coronary artery disease, left ventricular hypertrophy, atrial fibrillation, stroke, and CKD progression [40-43]. Moreover, approximately 25% of individuals with hyperuricemia exhibit MSU crystal deposition detectable by specialized imaging, even prior to the development of clinical gout [27]. Nevertheless, randomized trials have inconsistently demonstrated clinical benefits from treating asymptomatic cases, although urate-lowering therapy may offer advantages for specific high-risk populations [5, 43]. Given these facts, alongside the data presented in this review, further investigation into cardiac valve involvement in asymptomatic hyperuricemic patients is highly warranted.

4. Conclusions

The growing number of histologically confirmed case reports, combined with DECT data revealing a significant percentage of imaging-detected MSU deposits in cardiac valves - two related but non-equivalent lines of evidence - warrants increased clinical and scientific attention to valvular involvement in both overtly gouty and hyperuricemic individuals, although these observations remain preliminary and should be interpreted with caution given the limited and heterogeneous evidence base.

Declarations

Author Contributions

All authors contributed to the study conception and design. BP performed the literature review and was responsible for drafting, editing, and revising the manuscript, as well as participating in the clinical management of the patient. GS and VG contributed to the editing and critical revision of the manuscript at all stages of production. All authors gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author used LLM Gemini (Google Inc.) to improve the overall language and readability of the manuscript. Additionally, generative AI was used to draft the initial versions of the abstract and the section summarizing the article “Dual-Energy Computed Tomography Detection of Cardiovascular Monosodium Urate Deposits in Patients With Gout”. After using these tools, the authors carefully reviewed, edited, and verified all content, and take full responsibility for the accuracy, originality, and final content of the publication.

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Institutional Review Board Statement

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Data Availability Statement

The data presented in this study are available on reasonable request from the corresponding author.

Conflicts of Interest

The authors declare no conflict of interest.

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