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A Comparative Review of European and American Guidelines for Marker-Negative Intratesticular Lesions: One Testicular Mass, Two Pathways?

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Abstract

The management of a small intratesticular mass depends on whether it is genuinely indeterminate or suspicious for malignancy; normal serum tumour markers do not resolve that distinction. This narrative review compares the European Association of Urology (EAU) 2026- and American Urological Association (AUA) 2023-amended recommendations and examines the evidence supporting surveillance, additional imaging and testis-sparing surgery. Official guidelines and relevant clinical studies were reviewed through 12 October 2026, with attention to enrolment phenotype, histological verification and procedural sampling. Both guidelines favour radical inguinal orchidectomy for a mass considered malignant. For indeterminate findings with normal alpha-fetoprotein and human chorionic gonadotrophin, the AUA specifies repeat imaging after six to eight weeks and sets explicit eligibility criteria for testis-sparing surgery; the EAU supports selective magnetic resonance imaging and enucleation with frozen-section examination in appropriately selected masses. Surveillance cohorts largely comprise incidental, non-palpable lesions below 1 cm. Their low observed event rates cannot be extrapolated to symptomatic, enlarging or otherwise suspicious masses. Imaging accuracy studies assess characterisation, not comparative patient outcomes from competing pathways, while high frozen-section accuracy derives from targeted excisional sampling. Inflammatory disease may mimic a neoplasm or coexist with one; a benign result from limited tissue does not necessarily account for a persistently suspicious radiological target. Guideline interpretation should therefore begin with lesion phenotype and, when pathology and imaging disagree, return to whether the relevant abnormality was adequately represented.

Categories: Urology
Keywords: clinical practice guideline, diagnostic discordance, frozen section, intratesticular lesion, orchidectomy, small testicular mass, testis-sparing surgery, ultrasonography

Introduction And Background

High-resolution scrotal ultrasonography increasingly detects small intratesticular abnormalities during investigations for infertility, pain and unrelated scrotal conditions. For this review, an incidental lesion is one found unexpectedly, often non-palpable and asymptomatic; an indeterminate lesion is one for which examination and imaging do not establish a sufficiently confident benign or malignant diagnosis; and a suspicious lesion has clinical or imaging features that raise substantive concern for neoplasm, irrespective of serum-marker results. These categories are not interchangeable: a lesion can be incidentally discovered yet radiologically suspicious. Normal alpha-fetoprotein (AFP) and human chorionic gonadotrophin (hCG) exclude neither seminoma nor other marker-negative germ-cell malignancy. Histology series show that many selected small incidental lesions are benign, prompting interest in surveillance and testis-sparing surgery (TSS); nevertheless, such evidence cannot be generalised automatically to a vascular, palpable, enlarging or otherwise suspicious mass [1-3].

The European Association of Urology (EAU) and American Urological Association (AUA) share radical inguinal orchidectomy as the standard treatment for a suspicious testicular malignancy while permitting selected preservation strategies [1,4]. Tozzi and colleagues have already compared five international guidelines and formally appraised their quality [5]. Repeating their recommendation inventory would add little. This review instead examines three practical questions: how the EAU and AUA operationalise diagnostic uncertainty; which patients contributed to the evidence supporting observation, advanced imaging and frozen-section examination (FSE); and how reassuring limited pathology should be interpreted when imaging remains suspicious.

Review

Literature sources and approach

The EAU 2026 diagnostic-evaluation chapter and the AUA guideline published in 2019 and amended in 2023 were the primary sources [1,4]. A targeted, English-language narrative literature search of PubMed,

publisher full-text websites and cited reference lists was undertaken on 11-12 October 2026. Search concepts, used singly and in focused combinations, were as follows: "small testicular mass", "testicular incidentaloma", "indeterminate testicular lesion", "ultrasound surveillance", "testis-sparing surgery", "frozen section", "testicular MRI", "contrast-enhanced ultrasound", "orchitis", "testicular abscess", "seminoma" and "radiology pathology discordance". Relevant papers identified through citation tracking were also considered. The published guideline recommendations and numerical diagnostic accuracy estimates cited here were rechecked against their primary sources on 25 October 2026. Original database-wide Boolean strings and full retrieval counts were not archived for the initial targeted search; this is acknowledged rather than retrospectively reconstructed as a systematic search.

The narrative eligibility framework prioritised adult intratesticular masses; official clinical guidance; and peer-reviewed observational studies, accuracy studies, case-based pathology analyses and systematic reviews addressing imaging, incidentaloma surveillance, TSS/FSE or radiology-pathology discordance. Evidence with stated enrolment phenotype, denominators and reference standards was prioritised when numerical results were interpreted. Paediatric or exclusively extratesticular lesions, unrelated interventions and reports not informing these decisions were outside scope. Relevant citations were selected purposively, with interpretation organised by presentation phenotype, reference standard, evidence limitations and guideline decision point. This was not a protocol-registered systematic review: there was no exhaustive dual-review screening, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram, independent duplicate extraction, or formal study-level risk-of-bias scoring. No estimates were pooled across distinct patient groups; the resulting synthesis is descriptive and interpretative.

Where EAU and AUA recommendations diverge

Both organisations recommend scrotal ultrasonography and pre-treatment measurement of AFP, hCG and lactate dehydrogenase (LDH), and both favour inguinal orchidectomy once a solid lesion is judged suspicious for malignancy [1,4]. Normal markers do not exclude germ-cell cancer, particularly seminoma. The important qualification is the indication for a conservative pathway, rather than the presence of a numeric size threshold alone.

AUA Statement 6 specifies repeat imaging after six to eight weeks when AFP and hCG are normal and examination or ultrasonography is indeterminate. Statement 7 advises against magnetic resonance imaging (MRI) as the initial diagnostic investigation for a lesion suspicious for neoplasm. By contrast, the EAU does not prescribe a universal short-interval repeat-scan schedule and reserves MRI for inconclusive ultrasound, selected tumour characterisation or planning TSS. Both allow selected TSS, although the AUA specifies a lesion smaller than 2 cm alongside defined clinical conditions; the EAU is less prescriptive about a universal size threshold for small or indeterminate marker-negative lesions [1,4]. Table *1* sets out the operational differences without treating a difference in wording as a conflict in standard oncological care.

Clinical decision	EAU 2026	AUA 2023 amendment	Reading of the difference
Ultrasound and markers	Bilateral high-frequency ultrasound; AFP, hCG and LDH [1]	Doppler ultrasound; pre-treatment AFP, hCG and LDH [4]	Concordant initial assessment
Suspicious solid mass	Inguinal orchidectomy remains standard; avoid scrotal access [1]	Radical inguinal orchiectomy with a normal contralateral testis [4]	Concordant oncological default
Indeterminate finding	No universal 6-8-week initial reassessment interval or validated safe size cutoff [1]	Repeat imaging at 6-8 weeks if examination/ultrasound is indeterminate and AFP/hCG normal; Statement 6 [4]	AUA gives an explicit timetable for a restricted phenotype
MRI	Consider when ultrasound is inconclusive or to help characterise/select for TSS; not routine [1]	Not recommended as the initial diagnostic test for a suspicious lesion; Statement 7 [4]	Different emphasis; both place ultrasound first
TSS with normal opposite testis	Consider for suitable small or indeterminate, marker-negative lesions, with FSE [1]	May offer inguinal TSS in highly selected masses <2 cm with equivocal findings/negative markers or other qualifying circumstances; Statement 11a [4]	Overlapping preservation options; AUA eligibility is more explicit
FSE and subsequent pathology	FSE with TSS in experienced hands; definitive histology can require delayed orchidectomy [1]	Discuss FSE of the lesion and obtain additional normal parenchymal biopsies during TSS; Statements 11a-c [4]	Both depend on expert, representative excisional assessment
Benign limited biopsy but suspicious serial imaging	No dedicated algorithm for this exact sequence in the diagnostic chapter [1]	No dedicated post-limited-biopsy algorithm in the initial triage statements [4]	The absence of a specific post-biopsy algorithm does not supersede the standard approach to a persistently suspicious mass

TABLE 1: Comparison of guidance at the diagnostic decision points.

Recommendations are paraphrased. The AUA statement numbers refer to its 2023-amended guidance.

EAU: European Association of Urology; AUA: American Urological Association; AFP: alpha-fetoprotein; hCG: human chorionic gonadotrophin; LDH: lactate dehydrogenase; MRI: magnetic resonance imaging; TSS: testis-sparing surgery; FSE: frozen-section examination; cm: centimetres

The AUA repeat-imaging instruction is not a surveillance recommendation for every marker-negative solid mass. Its qualifying word is "indeterminate". Similarly, EAU consideration of TSS does not place an enlarging, radiologically malignant-appearing mass in the same group as a small lesion with a plausible benign explanation. The absence of a shared operational definition of indeterminate disease leaves room for variation in individual decisions, but neither guideline has demonstrated superior diagnostic outcomes in a directly comparable patient population [1,4,5].

Surveillance evidence: selection precedes outcome

Two types of evidence have driven increased interest in avoiding immediate orchidectomy. Henriques and colleagues reported that 41.1% of surgically excised small testicular masses across 57 studies were benign [2]. That figure concerns masses selected for surgery, not the pre-test probability in all masses seen on ultrasound. Separately, the EAU 2026 guideline summarises a high benign proportion for very small incidental lesions, citing 70% benignity among lesions smaller than 10 mm while emphasising that no individual ultrasound feature is fully reliable [1]. Neither estimate is applicable without qualification to a progressive, symptomatic or multifocal vascular testicular mass. Reviews specifically of small, incidentally detected, non-palpable lesions further demonstrate why enrolment phenotype must be considered before extrapolating surveillance evidence [3,6].

Bieniek and colleagues identified 120 subcm masses among 4,088 men undergoing ultrasonography for infertility [7]. Eighteen men underwent surgery during a mean follow-up of 1.3 years; six had seminoma. The other 102 remained under observation at the last assessment, without a tissue diagnosis. Each malignant lesion measured more than 5 mm and was vascular at baseline, but neither size nor vascularity significantly separated malignant and benign lesions among those operated on. The study documents the feasibility of

surveillance for selected infertility-associated incidentalomas; it cannot estimate the false-negative rate of observation in patients presenting with a progressive symptomatic mass.

Bertolotto and colleagues followed 130 incidental, non-palpable, marker-negative solid lesions smaller than 1 cm at seven centres [8]. Twenty-eight enlarged and all underwent surgery; 18 were malignant, while 10 had benign or non-neoplastic histology. Among the 102 remaining lesions, six disappeared, eight shrank, and 88 were stable. Thirty-seven patients had more than one small lesion, but only the largest was analysed. Consequently, multifocality was not absent from the study population; what remains untested is surveillance of multiple larger, independently suspicious foci. Moreover, 18 malignancies among the 28 growing operated lesions are not an overall prevalence estimate: surgery preferentially verified lesions behaving suspiciously, while most stable lesions were not sampled.

Brown and colleagues' surveillance review comprised 293 selected patients, of whom 37 underwent surgical exploration and 10 were diagnosed with malignancy [9]. Its event fractions describe clinical outcomes under heterogeneous observation policies, not the cancer probability associated with a newly discovered marker-negative solid lesion. Taken together, these studies support structured observation for carefully selected incidentalomas and justify escalation when enlargement or a concerning phenotype emerges. They do not provide a validated threshold of size, vascularity or growth at which malignancy can be confidently excluded [1,7-9].

Advanced imaging: characterisation rather than pathway superiority

The European Society of Urogenital Radiology and subsequent imaging reviews describe a role for additional characterisation when conventional Doppler ultrasound cannot distinguish a benign mimic from malignancy [10-13]. In a prospective single-centre study, Törzsök and colleagues examined 48 surgically selected patients with equivocal ultrasound; 35 had malignant histology [14]. Multiparametric MRI sensitivity was 94.3% (95% confidence interval (CI): 80.8-99.3%) and specificity 76.9% (95% CI: 46.2-95%), using surgical histopathology as the reference standard. The high prevalence of malignancy and the surgically selected setting preclude direct generalisation to tiny incidental nodules that would otherwise be observed.

The 2026 meta-analysis by Ibis and colleagues included 12 studies, 912 patients and 920 lesions [15]. Across distinct source-study populations, MRI had a pooled sensitivity of 94% (95% CI: 88-97%) and a specificity of 84% (95% CI: 72-91%), while contrast-enhanced ultrasound (CEUS) had a pooled sensitivity of 90% (95% CI: 80-95%) and a specificity of 74% (95% CI: 47-91%). These were indirect across-study estimates, not the accuracy of both modalities tested head-to-head in the same patients. Reference standards included histology and, in some contributing studies, longitudinal follow-up. Heterogeneity of enrolment, verification and protocols limits between-modality interpretation and precludes claims that an MRI-first clinical pathway prevents delayed cancer diagnosis or unnecessary orchidectomy more effectively than interval ultrasonography [1,4,15].

Preservation surgery and the limits of frozen-section performance

EAU and AUA support TSS in selected patients where preservation of endocrine or reproductive function is important and the lesion can be excised appropriately [1,4]. The AUA confines its conditional recommendation to a mass smaller than 2 cm with an additional qualifying circumstance, including equivocal imaging/examination with negative AFP and hCG. The EAU permits consideration of enucleation in selected small or indeterminate marker-negative masses despite a normal contralateral testis, with FSE used to guide management. The choice depends not just on diameter but on the location and number of targets, residual parenchymal volume and availability of experienced intraoperative pathology [1,4,16,17].

The diagnostic performance of FSE is compelling within that excisional workflow. EAU cites a sensitivity of 99% and a specificity of 96% in expert hands [1]. In Choiniere and colleagues' specialist-centre series of 135 excisional frozen sections (median mass diameter 0.9 cm), 51 lesions were malignant on definitive histology [18]. Three intraoperative results were indeterminate. Among the other 132, frozen and permanent diagnoses agreed in 129 (97.7%); sensitivity and specificity for malignancy were 100% and 96.3%, with three false positives and no false negatives. These observations are consistent with earlier specialist experience [19], but do not assess whether a small fragment is representative of a radiologically heterogeneous testis.

Four processes must be distinguished when reassuring tissue findings later prove incomplete: sampling a site other than the radiological target; tumour present in the paraffin block but absent from initial examined levels; atypia obscured by necrosis or inflammatory artefact; and misinterpretation despite tumour being present and recognisable on the original slides. Only the last is straightforward interpretative error. The appropriate response to persistent suspicion is to reconcile the original lesion map with the tissue obtained, review specimen representativeness and consider specialist pathology review, deeper tissue levels or indicated immunohistochemistry, alongside repeat imaging or oncological management as clinically appropriate [18,20-22]. Ipsilateral background biopsies recommended by the AUA during TSS assess germ-cell neoplasia in situ and do not compensate for inadequate sampling of the main lesion [4]. Accuracy from complete lesion enucleation cannot be assumed for an incisional or abscess-directed fragment [17-19].

Longer-term outcomes after TSS are relevant because preservation avoids the removal of testicular tissue but introduces potential local recurrence, repeat treatment and ongoing surveillance obligations. A systematic review by Favilla and colleagues considered oncological and functional outcomes after TSS for small masses [17], while AUA guidance explicitly requires counselling about local recurrence, serial examination and ultrasonography, possible adjuvant radiotherapy, testicular atrophy, testosterone deficiency and impaired fertility [4]. The studies vary in lesion pathology, patient selection and follow-up duration; they do not provide a directly comparable long-term advantage for one guideline pathway over another. Endocrine, fertility and patient-reported outcomes should therefore be described as important considerations, not presumed benefits for every patient.

Table *2* consolidates the studies that most directly inform observation, advanced imaging and FSE, with the population limits that govern clinical interpretation.

Study	Study population/finding	What can be inferred	Boundary of applicability
Bieniek et al. [7]	120 incidental lesions <10 mm in men undergoing infertility ultrasound; six seminomas among 18 operations	Follow-up can be feasible in selected incidentalomas	Histology absent for 102 observed lesions; not a symptomatic progression cohort
Bertolotto et al. [8]	130 incidental, non-palpable lesions <10 mm; 37 patients with multiple foci; 18 cancers among 28 growing lesions	Growth is an escalation signal, not a malignant diagnosis	Largest lesion analysed; growth-driven histology creates verification bias
Brown et al. [9]	293 selected patients initially surveilled; 37 explored, 10 malignant	Observation outcomes in carefully selected series	Heterogeneous inclusion, follow-up, interventions and verification
Törzsök et al. [14]	48 surgically selected equivocal lesions (35 malignant); MRI sensitivity 94.3% (95% CI: 80.8-99.3%) and specificity 76.9% (95% CI: 46.2-95%)	MRI can help with selected preoperative characterisation	High-prevalence surgical cohort; no management-strategy comparison
Ibis et al. [15]	12 studies/920 lesions: MRI sensitivity 94% (95% CI: 88-97%) and specificity 84% (72-91%); CEUS sensitivity 90% (80-95%) and specificity 74% (47-91%)	Both adjunctive modalities show useful diagnostic performance	MRI and CEUS estimates derive from different study populations, with mixed reference standards; they cannot be directly compared as paired tests or diagnostic pathways
Choiniere et al. [18]	135 targeted excisional FSEs; 129/132 conclusive frozen diagnoses concordant; no false negatives	High accuracy within specialist excisional practice	Does not evaluate limited incisional sampling or multiple unsampled foci
Nasu and Kawago [21]	Single culture-confirmed testicular abscess coexisting with seminoma	True infection and neoplasm can coexist	Cannot estimate prevalence or justify routine tumour surgery in orchitis

TABLE 2: Transferability of the principal clinical studies.

Study results reflect different enrolled populations and histological versus follow-up reference standards. MRI and CEUS pooled estimates are not derived from paired tests in the same individuals and must not be directly compared as alternative management pathways.

MRI: magnetic resonance imaging; CEUS: contrast-enhanced ultrasound; FSE: frozen-section examination; mm: millimetres; CI: confidence interval

Inflammation and the problem of discordant pathology

Pain and focal inflammation complicate imaging interpretation because orchitis may produce a hypoechoic, hypervascular focus that resembles neoplasia; infarction, haematoma and granulomatous change create further overlap [12,20,22]. A mature abscess typically contains an avascular or non-enhancing central component with surrounding hyperaemia, but imaging appearances vary with disease stage. An inflammatory presentation is therefore neither a diagnosis of cancer nor a reliable reason to exclude it. Nasu and Kawago reported seminoma coexisting with a microbiologically confirmed *Salmonella* testicular abscess [21]. This establishes that infection and cancer can coexist but provides no estimate of frequency.

When pathology appears benign or inflammatory but imaging remains suspicious, the essential question is

whether the examined specimen adequately represents the imaged abnormality. This requires review of targeting, specimen volume and the original imaging phenotype, with further specialist radiology-pathology discussion as appropriate. Neither EAU nor AUA specifies a dedicated post-limited-biopsy algorithm for this precise situation; both retain the broader principle that a suspicious lesion warrants definitive oncological assessment [1,4]. These diagnostic safeguards are evidence-informed clinical reasoning, not a prospectively validated management pathway.

Implications for clinical decisions and future research

Table *3* applies the published recommendations to four illustrative presentations. These are hypothetical clinical phenotypes, not patient case reports or a validated risk score; they show how the presentation at entry changes the relevance of supporting evidence.

Illustrative presentation	Guideline-concordant options	Evidence-based qualification
Non-palpable 4-mm incidental avascular nodule; normal markers	Specialist review; interval ultrasound may be selected after counselling [1,4,9]	Small-incidentaloma surveillance cohorts are most applicable, but malignancy is not impossible
Single equivocal 12-mm lesion; normal markers and opposite testis	AUA: repeat imaging at 6-8 weeks if truly indeterminate. Consider selected adjunctive MRI or inguinal TSS/FSE when appropriate [1,4]	Conservative approaches overlap; no direct comparative outcome trial identifies a superior sequence
Enlarging vascular mass or multiple evolving suspicious foci; normal markers	Urgent specialist oncological assessment; inguinal orchidectomy is usual if suspicion is high [1,4]	Marker negativity and an individual focus below 2 cm do not make a suspicious lesion an incidentaloma
Persistent concerning imaging after limited inflammatory tissue	Review imaging target and sampled tissue; GU pathology and appropriate definitive oncological reassessment [1,4,18,20]	An evidence-informed approach to unresolved discordance, not a stated guideline algorithm

TABLE 3: Application of guideline principles to illustrative clinical phenotypes.

These scenarios are hypothetical clinical examples, not observations from the authors' patients or a validated triage instrument.

AUA: American Urological Association; MRI: magnetic resonance imaging; TSS: testis-sparing surgery; FSE: frozen-section examination; GU: genitourinary; mm: millimetres

Future studies should record the means of discovery, palpability, the size and vascularity of each lesion, change on serial imaging, local expertise and completeness of tissue excision. Pathology studies should distinguish an unsampled target from a tumour absent at initial block levels or an interpretation error. Comparative studies of genuinely indeterminate lesions should measure delayed cancer diagnosis, unnecessary orchidectomy, endocrine and fertility outcomes, resource use and patient preference rather than diagnostic accuracy alone. No available study permits a claim that the EAU or AUA pathway is less expensive or more reliable in otherwise equivalent patients [5,8,15,18].

Limitations of this review

This targeted narrative review was not systematic and may omit relevant evidence. It did not independently appraise guideline quality, which has recently been examined in a dedicated international comparison [5]. Observational cohorts preferentially obtain histology from growing or suspicious lesions; accuracy studies use different clinical spectra and reference standards. The postoperative pathology-discordance literature is limited, and recommendations for re-review are extrapolated from sampling principles and broader oncological guidance rather than tested in prospective comparative studies. No patient data were analysed, and no new triage tool was developed or validated.

Conclusions

European and American recommendations are closely aligned for a testicular mass considered suspicious for malignancy. Their practical differences concern genuinely indeterminate findings: the AUA specifies an early repeat-imaging interval and explicit preservation criteria, while the EAU permits selected MRI characterisation and TSS with FSE. Surveillance evidence pertains mainly to small incidental, non-palpable lesions; MRI performance reflects selected imaging cohorts; and frozen-section accuracy reflects representative excisional specimens. None provides grounds for dismissing progressive suspicious imaging because serum markers are normal or limited tissue shows inflammation. When radiology and pathology remain discordant, the next decision should address whether the imaged lesion was adequately represented

and whether the subsequent clinical course still supports a benign diagnosis.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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