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Title: An image-guided diagnostic pathway for undiagnosed pleural exudates

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Body: Background: We assessed the efficiency and safety of an image-guided diagnostic pathway with ultrasound (US)-assisted closed pleural biopsy as an alternative to thoracoscopy as first-line investigation in undiagnosed pleural exudates. Methods: Patients with non-diagnostic thoracocentesis were prospectively stratified on imaging as having (A) an associated mass lesion (>10mm) abutting the chest wall; (B) diffuse pleural thickening (>10mm) and/or nodularity or (C) insignificant/no pleural thickening. US-assisted repeat thoracocentesis and transthoracic fine-needle aspiration were performed on patients stratified to (A), and if non-diagnostic on on-site analysis, a Tru-Cut biopsy was performed in the same session. US-assisted thoracocentesis and Abrams needle biopsies were performed on all others aiming at the region(s) of interest (B) or low supra-diaphragmatic pleura (C). Thoracoscopy was reserved for cases not diagnosed by repeat thoracentesis and biopsy. Results: Final diagnoses in 78 consecutive patients included malignancy (n=42), TB (n=30), and other causes (n=6). Accurate diagnoses were obtained in 69 (88.5%) with US-assisted thoracocentesis and biopsy. The yield was high for TB (93.3%) and malignancy (88.1%). Complications included mild haemoptysis (n=1) and pneumothorax (n=1, no intervention required). Thoracoscopy was performed in 13 cases (16.7%), including all 4 cases correctly diagnosed on closed biopsy as non-specific pleuritis, and yielded diagnoses in 12. Conclusion: A diagnostic algorithm based on pleural morphology, US-assisted thoracocentesis and biopsy has a high diagnostic yield and offers an efficient and safe alternative to thoracoscopy as a first-line investigation in undiagnosed exudates.