

Breathomics in mesothelioma detection: volatile organic compounds-based approach for rapid and non-invasive diagnosis: a systematic review and meta analysis

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ABSTRACT

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Malignant pleural mesothelioma (MPM) is a rare but fatal cancer linked to asbestos exposure, accounting for over 30,000 deaths annually with a median survival of less than 12 months. Its prolonged latency (30 – 40 years) and non-specific symptoms, early diagnosis challenging. Breath analysis of volatile organic compounds (VOCs) offers a non-invasive method potentially capable of detecting MPM before radiologic signs appear. This meta-analysis evaluates the diagnostic accuracy of VOC-based breathomics in MPM detection from healthy controls (HC), asbestos-exposed individuals (AE), and other asbestos-related diseases (ARD). A systematic search of PubMed, Scopus, Web of Science, Google Scholar, and ScienceDirect identified 2,956 articles, of which six cross-sectional studies (n=618) met PRISMA-based inclusion criteria: (1) VOC-based breath analysis using GC-MS, MCC/IMS, CDA-PCA, or e-nose; (2) reporting diagnostic accuracy metrics (Sn, Sp, AUC, PPV, NPV); (3) including MPM, HC, and AE groups; and (4) comparison with standard diagnostic references. Risk of bias was assessed via QUADAS-2; publication bias with funnel plots and Egger's test; and bivariate meta-analysis conducted using REML in R. Compared to HC, VOC-breathomics yielded a sensitivity of 0.830, specificity of 0.686, and AUC of 0.786 ($I^2 \approx 29.1\%$). Against AE and ARD, sensitivity was 0.877 and 0.807; specificity was 0.850 and 0.723; AUC was 0.860 and 0.815 ($I^2 \approx 0\%$). LogDORs were 2.86 [1.75-3.96] (HC), 3.42 [2.33-4.52] (AE), and 2.72 [1.90-3.53] (ARD). Publication bias was detected for HC ($p=0.0464$) but not AE/ARD. VOCs such as cyclohexane, benzonitrile, and α -pinene have been identified as markers for MPM and lung cancer. While cyclopentane, methyl-octane, and dimethyl-nonane are good indicators for long-term asbestos exposure. VOCs from breath analysis show strong potential for early and non-invasive MPM diagnosis. VOC-based breath analysis has great potential as a non-invasive method for early detection of MPM, although large-scale validation studies are still needed.

ABSTRAK

Mesothelioma pleura maligna (MPM) merupakan kanker langka namun fatal yang terkait dengan paparan asbes, menyebabkan lebih dari 30.000 kematian per tahun dengan median kelangsungan hidup kurang dari 12 bulan. Masa laten yang panjang (30–40 tahun) serta gejala yang tidak spesifik menyebabkan diagnosis dini sulit ditegakkan. Analisis napas terhadap senyawa organik volatil (*volatile organic compounds*; VOCs) menawarkan pendekatan non-invasif yang berpotensi mendeteksi MPM bahkan sebelum tanda radiologis muncul. Meta-analisis ini bertujuan mengevaluasi akurasi diagnostik *breathomics* berbasis VOC dalam deteksi MPM dari individu sehat (HC), individu terpapar asbes (AE), dan penyakit terkait asbes lainnya (ARD). Pencarian sistematis pada PubMed, Scopus, Web of Science, Google Scholar, dan ScienceDirect mengidentifikasi 2.956 artikel, dengan enam studi *cross-sectional* (n=618) yang memenuhi kriteria inklusi berbasis PRISMA: (1) analisis napas dilakukan menggunakan GC-MS, MCC/IMS, CDA-PCA, atau *electronic nose*; (2) pelaporan metrik akurasi diagnostik (Sn, Sp, AUC, PPV, NPV); (3) termasuk kelompok MPM, HC, dan AE; dan (4) perbandingan dengan referensi diagnostik standar. Risiko bias dievaluasi dengan QUADAS-2, bias publikasi dengan funnel plot dan uji Egger; dan meta-analisis bivariat menggunakan REML. Dibandingkan dengan HC, analisis VOC

Keywords:

Breath Analysis;
Mesothelioma;
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menunjukkan sensitivitas 0,830, spesifisitas 0,686, dan AUC 0,786 ($I^2 \approx 29,1\%$). Dibandingkan dengan AE dan ARD, sensitivitas masing-masing adalah 0,877 dan 0,807, dengan spesifisitas 0,850 dan 0,723, serta AUC 0,860 dan 0,815 ($I^2 \approx 0\%$). Nilai LogDOR adalah 2,86 [1.75-3.96] (HC), 3,42 [2.33-4.52](AE), dan 2,72 [1.90-3.53](ARD). Bias publikasi terdeteksi untuk HC ($p=0,0464$) tetapi tidak untuk AE/ARD. VOC seperti sikloheksana, benzonitril, dan α -pinena diidentifikasi sebagai penanda MPM dan kanker paru-paru. Sementara itu siklopentana, metil-oktana, dan dimetil-nonana merupakan indikator yang baik untuk paparan asbes jangka panjang. Analisis napas berbasis VOC memiliki potensi besar sebagai metode non-invasif untuk deteksi dini MPM, meskipun studi validasi berskala besar masih diperlukan.