

Evidence Discussion (ONC 30.1)

Fever of Unknown Origin

The widely accepted definition of “Fever of Unknown Origin” is persistent fever of at least 101 degrees F for at least 3 weeks with unidentified cause. Most published recommendations are based on expert consensus rather than data. Malignancy accounts for 20-30% of FUO in adults (David 2022, Wright 2020). The remainder are infectious, inflammatory, and immune mediated. Physical exam, CXR and laboratory findings including workup for specific infections should guide workup, and all routine age- based cancer screening should be complete. If these are negative, further workup may be indicated. Echocardiogram, abdominal ultrasound, and MRI brain without and with contrast are supported, with sensitivity rates of 80-86%, as abdominal and pelvic abscess, endocarditis, and viral and bacterial CNS processes remain more common causes of fever than malignancy. (David 2022, Bleeker-Rovers 2007, Wright 2020). These modalities limit radiation exposure and are recommended as first line imaging in most algorithms (David 2022, Wright 2020, Bleeker-Rovers 2007).

If the above workup has not demonstrated a source of infection, CT with contrast of the chest, abdomen and pelvis is supported as second line imaging, with sensitivity of up to 90% and specificity up to 70% for determining the cause of fever (Davis 2022, Wright 2020) . Technitium-based scans are insensitive but highly specific (93-94%), with the advantage of lower radiation exposure than CT, and are supported to localize infectious or inflammatory foci (David 2022, Hayakawa 2016, Takeuchi 2016). MRI brain without and with contrast is supported for any CNS symptoms accompanied by fever, as supported by several FUO algorithms and as outlined in eviCore HD 14.1 CNS and head infection. B symptoms with concern for lymphoma also warrant CTs, with further details outlined in eviCore ONC 27.1. The utility of PET/CT in workup of FUO is emerging, but specificity is variable, ranging from 52-85% (Bleeker-Rovers 2007, Kan 2019, Takeuchi 2016, Minamimoto 2022, Palestro 2023) At this time it is not routinely supported by eviCore guidelines in the workup of FUO.

References

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