degree as diagnostic tools and are showing promise for improving PMSI diagnosis.

Evidence for the diagnostic use of PCR in PMSI is sparse. In a prospective study exploring the utility of PCR, Verdier et al. enrolled 171 pediatric patients with osteoarticular infection (OAI). From this cohort, 64 culture-positive specimens were identified, of which 9 cases were positive for *Kingella kingae*. When the 107 culture-negative specimens were tested with PCR, 15 additional cases of *Kingella kingae* were detected [5]. Similarly, Chometon et al. conducted a study of 131 patients with acute pediatric OAI in a single hospital and found that pathogen identification improved from 45% by culture alone to 66% with both culture and PCR testing [6].

Ferroni et al. performed a prospective study with 197 acute pediatric OAI cases in a single hospital and found that the use of PCR in addition to culture and histology increased bacterial diagnosis by 54%.

There is additional evidence for the utility of PCR aiding diagnosis of musculoskeletal infection from studies examining adult cases. However, the reported sensitivity of PCR varies widely in the literature from 43.8% to 92.5% and specificity ranges from 92.9% to 100% [7–9]. Despite this variation, investigators consistently conclude that the rapid availability of the results (<1 day) make PCR an adjunctive tool for guiding early treatment prior to the availability of culture results [7,8], especially in the setting of a negative culture [9]. It should be noted that these studies used different standards to compare to PCR performance; Bonilla et al. and Fenollar et al. used culture results as their gold standard, while Fihman et al. used clinician diagnostic judgment based on predetermined factors [7,9]. This significant inconsistency renders the results difficult to compare and interpret across studies.

PCR has also shown promise as a valuable tool for diagnosing tuberculosis affecting the bones and joints [10–12]. *Mycobacterium tuberculosis* is a particularly difficult organism to culture because false-negative results are relatively common. Therefore, a rapid, reliable diagnostic test is still needed. A study of 24 samples (21 patients) showed that PCR had 100% sensitivity and 87.5% specificity for identifying tuberculous disease affecting the bones and joints. However, two false-positive results were seen in patients who had previously been diagnosed with tuberculosis [10].

An infected joint can rapidly progress into a medical emergency. Rapid molecular diagnostic tools could play a crucial role in identifying and treating the infection promptly [13]. PCR is a sensitive, rapid and widely-available molecular methodology that can detect microbial pathogens in clinical samples. However, in order to obtain reliable and consistent results it is necessary to standardize PCR preparation protocols and take care to avoid contamination [1,13].

Further research is needed to investigate the role that PCR and other molecular methods can play in identifying a pathogen.

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QUESTION 7: How can we differentiate between sickle cell crisis and septic arthritis/osteomyelitis (OM)?

RECOMMENDATION: A combination of clinical, laboratory and imaging studies are all needed for differentiating between sickle cell crisis and infection. A positive aspiration for infection from the joint or periosteum confirms the presence of infection while sequential ultrasounds in the absence of sub-periosteal fluid collection favor sickle cell crisis. Tri-phasic bone scan in the first 24 hours can differentiate vaso-occlusive crisis (VOC) from acute infection. Contrast-enhanced magnetic resonance imaging (MRI) is fairly accurate in differentiating infection from infarction.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 87%, Disagree: 0%, Abstain: 13% (Super Majority, Strong Consensus)

RATIONALE

Differentiating bone and joint infection from osteonecrosis (ON) in sickle cell disease (SCD) can be very challenging. Clinical presentation is an important tool in distinguishing OM from VOC in SCD: sudden, often severe pain; no or low-grade fever of less than 100 F (<38 c); inflam-

matory markers only mildly elevated; and elevated HB/HCT ratio are all indicative of crisis and ON [1–3]. Also, pain in more than one site is more likely to be a crisis and not OM [4,5].

Inusa et al. [6] in a retrospective study demonstrated that mean initial white blood cell count was 14.9 in VOC and 17.8 in OM. They reported mean C-reactive protein (CRP) as the more informative test in differentiating OM from VOC–86.4 vs. 39.8. Therefore, CRP should be included in the risk criteria for infection in an SCD patient with fever [7,8]. Radiographs in early phases of OM or VOC are usually normal, with periosteal reaction showing up in both conditions within the first 2 weeks [4,9].

Ultrasound scans alone can diagnose OM in SCD cases with 74% sensitivity and 63% specificity [10]. Ultrasound scan within the first six days shows periosteal elevation and/or fluid collection in 76% of OM, while 91% of VOC cases show no evidence of fluid collection. Repeat ultrasound is needed to confirm the diagnosis of VOC when fluid collection remains negative [6].

Combination of ultrasound and CRP was found to be a reliable, cost-effective measure in distinguishing OM from VOC [6]. Triphasic isotope bone scans and labeled WBC scans can be helpful in later stages [11–14]. Sequential radionuclide bone marrow scanning and bone scan within the first 24 hours differentiate bone infarction from acute infection [15,16].

T1-weighted MRI has low intensity in the medullary infarct and high intensity in T2-weighted images [4,11]. Contrast material enhancement on MRI may distinguish accurately between infection and infarction [17]. Un-enhanced bone marrow signal intensity on fat-saturated MRI images is not a reliable criterion for differentiation of infection from infarction according to Delgado [18].

Aspiration of pus from the subperiosteal region or joint, or positive blood culture remains the gold standard for diagnosing infection in SCD, bearing in mind that a negative blood culture does not rule out infection [8,19,20].

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