Risk of Infective Endocarditis in *Streptococcal mitis* Bloodstream Infections Among Patients with Neutropenia from Hematologic Malignancies

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Background

- *Streptococcus mitis* is a common colonizer of the human oral and gastrointestinal tract
- Patients with neutropenia due to hematologic malignancy (HM), particularly those prescribed fluroquinolone (FQ) prophylaxis, are at increased risk of a *S. mitis* bloodstream infection (BSI)[1]
- Risk of infective endocarditis (IE) in this patient population remains unclear

Purpose

- Describe risk of infective endocarditis among patients with neutropenia from hematologic malignancies who develop streptococcal mitis bloodstream infections

Outcomes

- The primary outcome was the number of patients who developed IE diagnosed on cardiac imaging
  - Transthoracic echocardiogram (TTE)
  - Transesophageal echocardiogram (TEE)
  - Cardiac computed tomography (CT)
- Secondary outcomes included number of patients who underwent IE workup via cardiac imaging, number of patients treated empirically for endocarditis (i.e., >2 weeks), BSI recurrence within 12 weeks of initial date of blood culture clearance, rates of fluoroquinolone and penicillin resistance, and duration of therapy

Methods

Design: Multicenter (Brigham and Women's Hospital, Massachusetts General Hospital, and Dana-Farber Cancer Institute), retrospective cohort study (July 2015 – February 2022)

Inclusion

- At least 1 positive blood culture with *S. mitis*
- Hematologic malignancy including acute leukemia, lymphoma, multiple myeloma, or chronic leukemia
- Neutropenia (≤500k/uL) within 48h of 1st positive blood culture

Exclusion:

- Clinical team considered the blood culture a contaminant
- Patient transitioned to hospice care during treatment for BSI
- ANC >500k/uL at time of positive blood culture

Results

Table 1 – Baseline characteristics	N = 207 (%)
Median Age – years (range)	59 (19-86)
Male Sex	123 (59)
Cancer Type	
• Acute leukemia/myelodysplastic syndrome*	160 (77)
• Lymphoma	33 (16)
• Multiple myeloma	11 (5)
• Chronic leukemia	3 (1)
Hematopoietic stem cell transplantation (HCT) before first (+) blood culture	120 (58)
Type of HCT	
• Autologous	28 (23)
• Allogeneic	92 (77)
History of IE	2 (1)
Baseline TTE Moderate or Severe Abnormality+	
• Prosthetic valve	0 (0)
• Aortic Valve (stenosis [n=3], regurgitation [n=1], bicuspid valve[n=1])	5 (3)
• Mitral Valve (regurgitation, n=1)	1 (0.6)
FQ prophylaxis within 24hr of positive blood culture	65 (31)
qSOFA – median (range)	0 (0-2)

* Chronic myelomonocytic leukemia, acute myeloid leukemia, acute lymphocytic leukemia, myelodysplastic syndrome, myelofibrosis

\+ Not all patients had baseline echocardiograms, n=177

Table 2 - Microbiology	N (%)
Polymicrobial	62 (30)
2 or more bottles positive on day 1 of positive blood culture	157 (76)
Blood culture cleared within 1 day of positive blood culture *^	161 (78)
Penicillin Intermediate or Resistant	73 (35)
Levofloxacin Intermediate or Resistant	82 (40)
• FQ in previous 90 days	67 (82)
• FQ in previous 24h	52 (63)

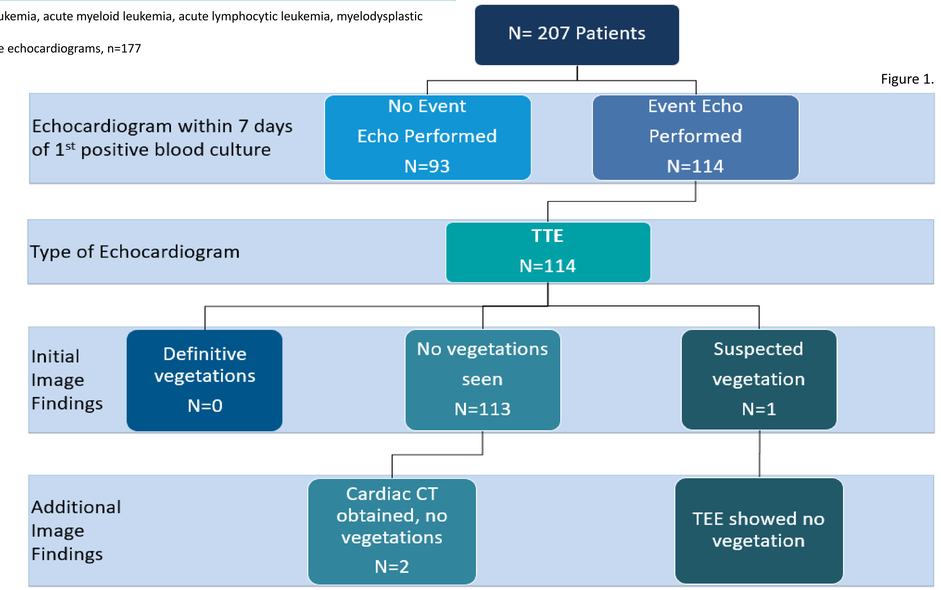
Table 3 - Outcomes	N (%)
Definitive endocarditis	0 (0)
Treated empirically for IE	1 (0.5)
TTE performed	114 (55)
Median duration of therapy – days (range, IQR) #	15 (5-43, 5)
Recurrence within 12 weeks of first positive culture#	3 (1.6)
Died during hospital admission	15 (7)

*1 patient did not have repeat blood cultures after initial set

^ Not all patients had repeat cultures taken the day after first positive culture

#n=192, the 15 patients who died during index hospital admission were excluded from recurrence and duration of therapy end points

Figure 1.



Results Summary

Among 207 patients who met inclusion criteria, 114 (55%) underwent cardiac imaging. All patients had native cardiac valves and **no cases of endocarditis were confirmed by imaging**

- Despite negative cardiac imaging (TTE, followed by CT), one patient completed 6 weeks of empiric vancomycin treatment for IE based on radiographic findings in the torso suggesting visceral infarcts given a *Staphylococcus schleiferi* & *S. mitis* BSI
- Three patients had *S. mitis* BSI recurrence within 12 weeks of first positive culture -- summarized below

Recurrence (n=3)	Time to Recurrence	TTE	Recurrence Treatment
Pulmonary nodules	11 wks	Negative	Empiric antifungal therapy & 4 week of ceftriaxone
GI Translocation	6.5 wks	Negative	2 weeks of linezolid
Metastatic colon cancer w/ liver lesions	10.5 wks	Negative	6 weeks of ertapenem

Conclusion

- *S. mitis* bacteremia is a common complication of neutropenia in patients with HM, particularly in those treated with quinolone prophylaxis
- While *S. mitis* may be associated with IE in the non-immunocompromised host population, we have shown that IE is uncommon in neutropenic HM patients with native cardiac valves and *S. mitis* BSI
- Recurrent BSI due to *S. mitis* was very rare in this cohort, suggesting IE cases were not under-diagnosed in those without cardiac imaging
- TTE does not appear to be necessary in the absence of persistently positive blood cultures or peripheral stigmata of endocarditis in this patient population

References

1. Han XY, Kamana M, Rolston KV. Viridans streptococci isolated by culture from blood of cancer patients: clinical and microbiologic analysis of 50 cases. J Clin Microbiol. 2006 Jan;44(1):160-5.
2. Chamat-Hedemand S, Dahl A, Østergaard L, Arpi M, Fosbøl E, Boel J, Oestergaard LB, Lauridsen TK, Gislason G, Torp-Pedersen C, Bruun NE. Prevalence of Infective Endocarditis in Streptococcal Bloodstream Infections Is Dependent on Streptococcal Species. Circulation. 2020 Aug 25;142(8):720-730.
3. Kim SL, Gordon SM, Shrestha NK. Distribution of streptococcal groups causing infective endocarditis: a descriptive study. *Diagn Microbiol Infect Dis*. 2018;91:269-272.

Disclosures: All authors have no financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation to disclose.