

## INTRODUCTION

A microbiological diagnosis is key to selecting appropriate antimicrobial therapy in infective endocarditis (IE). Molecular testing (16s rRNA sequencing and targeted PCR) of explanted valves could increase the sensitivity of identifying pathogens when compared with culture alone, particularly in IE caused by fastidious organisms or when cultures are taken after initiation of antimicrobial therapy.

A microbiological diagnosis can allow for optimisation of antibiotic therapy and may affect antimicrobial duration, which may lead to better treatment outcomes.

## OBJECTIVES AND METHODS

We identified 157 patients who underwent cardiac surgery for the management of IE over a 10-year period at Sheffield Teaching Hospitals, UK using a local cardiothoracic register. Surgical, microbiological and mortality data were collected on all patients including pre-operative blood-culture, valve culture and molecular testing (Micropathology Ltd, Warwick).

The principal aim of the project was to assess the clinical utility of performing different microbiological tests (i.e. culture or molecular testing) on valves by assessing the frequency valve investigations yielded a microbiological diagnosis compared to blood culture alone.

## RESULTS

We identified 157 patients who underwent cardiac surgery for infective endocarditis between 01/04/2012 to 31/12/2021. 127 of the 157 patients (81%) had native valve endocarditis, 24 (15%) had prosthetic valve endocarditis and in 6 (3%) this information was unavailable.

A microbiological diagnosis was made in 141 out of 157 patients who underwent surgery, with a range of organisms identified (table 1).

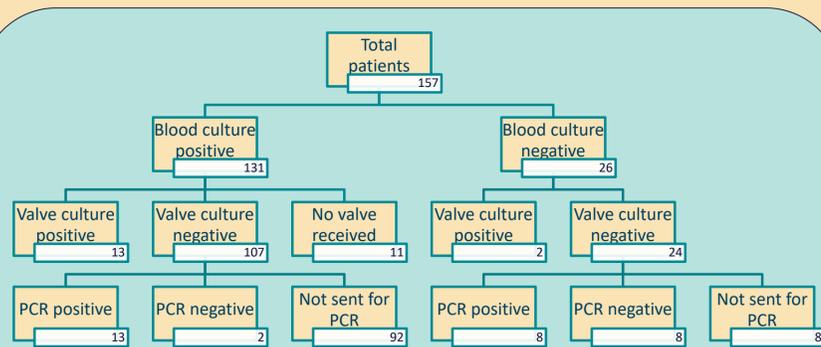
Organism	Total identified	1-year mortality
<i>Staphylococcus aureus</i>	49 (35%)	41%
Coagulase negative <i>Staphylococci</i>	10 (7%)	30%
Viridans group <i>Streptococci</i>	36 (26%)	19%
Other <i>Streptococci</i>	12 (9%)	33%
<i>Enterococci</i>	17 (12%)	29%
HACEK organisms	3 (2%)	33%
Other	12 (9%)	8%

**Table 1:** Cases in which a microbiological diagnosis was made categorised by organism identified.

146 patients (93%) had a valve sent for microbiological culture with 15 (10%) yielding a significant positive result (figure 1). 31 patients (21%) had valves sent for molecular testing (16s rRNA sequencing +/- specific PCR). Of these, 21 yielded a positive result (67%): 8 in patients with negative valve and blood cultures, 3 of these with fastidious organisms (*Bartonella quintana*, *Tropheryma whippelii* and *Cardiobacterium valvarum*).

8 patients who had negative valve and blood cultures had valves sent for molecular testing which yielded a negative result. We identified 8 patients who were culture negative who did not have their valve sent for molecular testing.

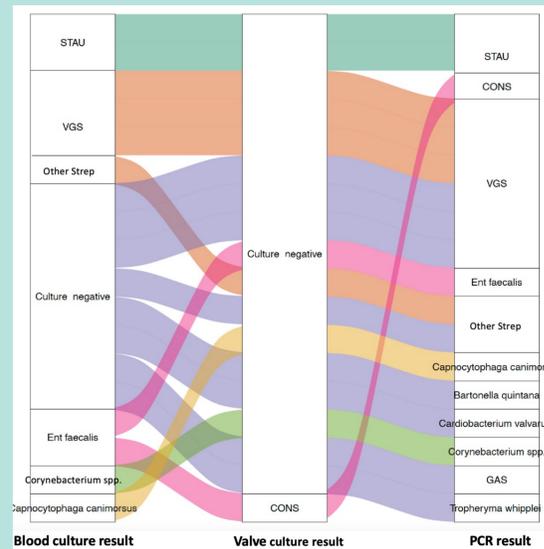
In patients with positive blood culture and positive molecular testing, there was concordance of results in 12 out of 13 cases.



**Figure 1:** Flowchart of patients categorised by result of blood culture, valve culture and molecular testing

The positivity rate for molecular testing was higher in mechanical valves compared with native valves (4 out of 4 prosthetic valves, 100% vs 17 out of 27 native valves, 63%;  $p = 0.20$ ).

1-year mortality rate of the overall cohort was 12.9%. Mortality was higher in those who had prosthetic valve infective endocarditis (41% vs 24%,  $p = 0.08$ ). 1-year mortality varied based on the identified organism, being highest when *Staphylococcus aureus* was identified (41%), and lowest with Viridans group *Streptococci* (19%).



**Figure 2:** Flow chart of blood culture, valve culture and molecular testing result for all patients who ultimately had positive molecular testing (n = 21), demonstrating results at each stage.

### Case study 1:

Middle aged female. Presented with breathlessness.

Multiple negative blood cultures.

Echocardiogram demonstrated multiple vegetations on the aortic and mitral valve, which both required surgical replacement.

Commenced on ceftriaxone for culture-negative endocarditis. Valve 16s rRNA and specific PCR positive for *Bartonella* species.

Antibiotics therefore changed to doxycycline and gentamicin as per ESC endocarditis guidelines.

### Case study 2:

Adult male who injects drugs. Admitted septic with multi-organ failure.

Antibiotics commenced prior to taking of blood cultures. Multiple subsequent negative blood cultures

Echocardiography demonstrated aortic root abscess. Underwent aortic valve and root replacement.

Initially commenced on vancomycin, flucloxacillin and gentamicin.

Valve culture negative. Valve 16s rRNA and specific PCR positive from *Streptococcus pyogenes*. Antibiotics changed to ceftriaxone alone.

## Discussion

Our retrospective evaluation of all patients who underwent cardiac surgery for endocarditis demonstrated a high degree of heterogeneity in the microbiological testing performed on explanted heart valves. There was no consistent criteria for which valves underwent molecular testing, nor for which molecular tests were requested. Of particular note, 8 of the 157 patients did not have molecular testing performed on their explanted valve despite being blood culture and valve culture negative.

Our analysis demonstrated that molecular testing was clinically useful and the number of patients lacking a microbiological diagnosis was halved when valves were sent for molecular testing. We demonstrated cases where gaining a microbiological diagnosis via molecular testing had a material effect on patient management by leading to a change in antimicrobial therapy, allowing for regimens with fewer adverse effects such as nephrotoxicity, *C. difficile* associated diarrhoea risk or development of antimicrobial resistance.

In conclusion, a standardised approach to the processing of explanted heart valves, particularly in blood-culture negative patients, increases rates of a positive microbiological diagnosis in IE, both for native and mechanical valves, which may improve outcomes.

### References:

Habib G, et al. ESC Guidelines for the management of infective endocarditis. Eur Heart J. 2015 Nov 21;36(44):3075-3128  
Shrestha NK, et al. Heart valve culture and sequencing to identify the infective endocarditis pathogen in surgically treated patients. Ann Thorac Surg. 2015 Jan;99(1):33-7