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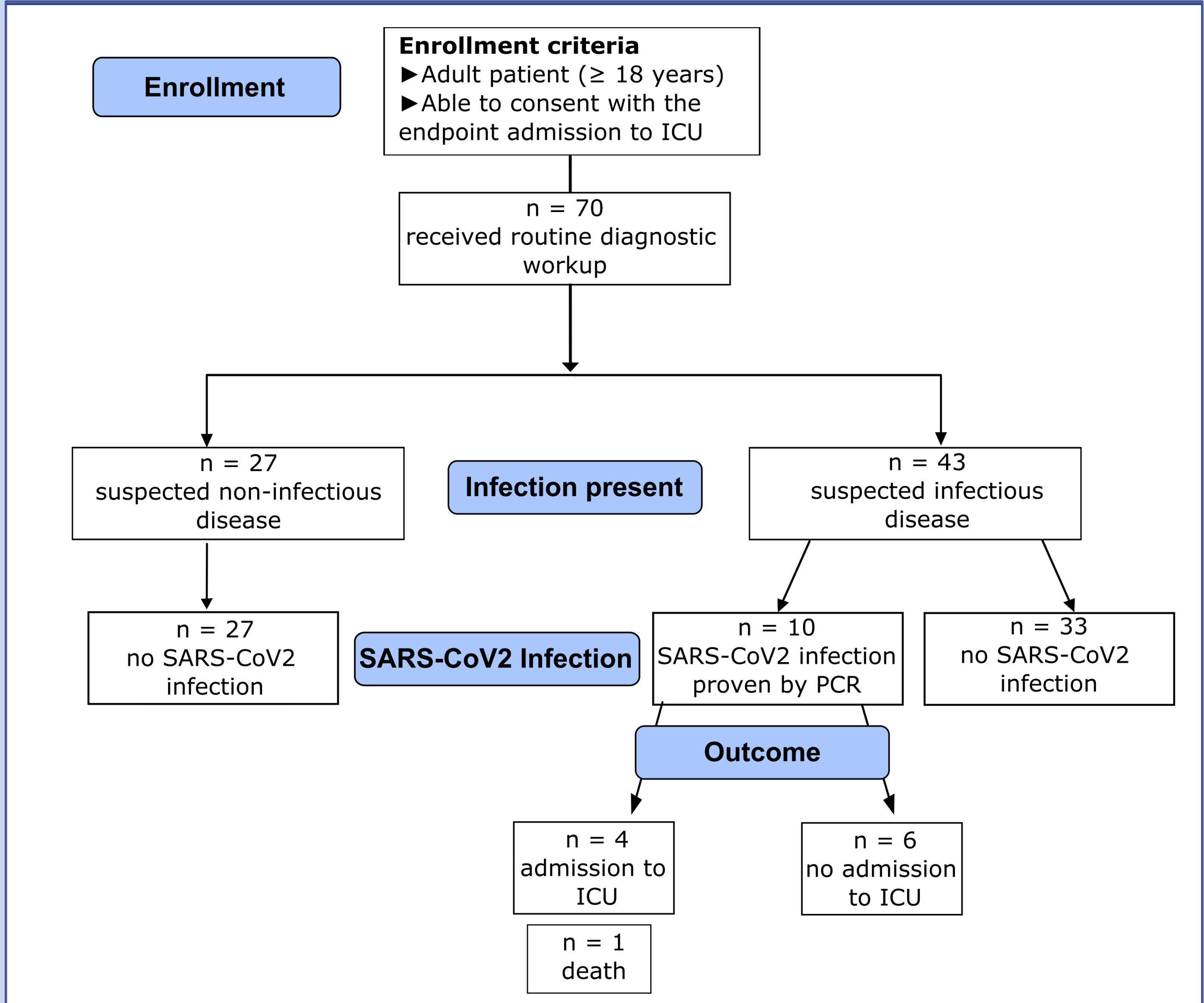
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Background:

COVID-19 is associated with a wide range of manifestations. Especially in the emergency department (ED) it is vital to identify patients with a high risk for development of multi-organ failure. Calprotectin is a novel biomarker found in the intracellular compartment of cells of the granulomonocytic lineage<sup>1</sup>. We recently identified serum calprotectin levels to be an excellent predictor of multi-organ failure, need for intensive care unit (ICU) treatment and death<sup>2</sup>.

Patients and Methods:

This analysis of an ongoing prospective controlled trial (CASCADE) was performed in the ED of the Charité – Universitätsmedizin Berlin Campus Benjamin Franklin from the beginning of February 2021. We have so far investigated a cohort of 70 patients, 43 with suspected infections and 27 with suspected non-infectious illness with 10 cases of COVID-19 proven by PCR.



**Fig. 1:** Enrollment of the CASCADE trial, recruitment until May 2021.  
ICU = Intensive Care Unit; n = Number of participants; PCR = Polymerase Chain Reaction

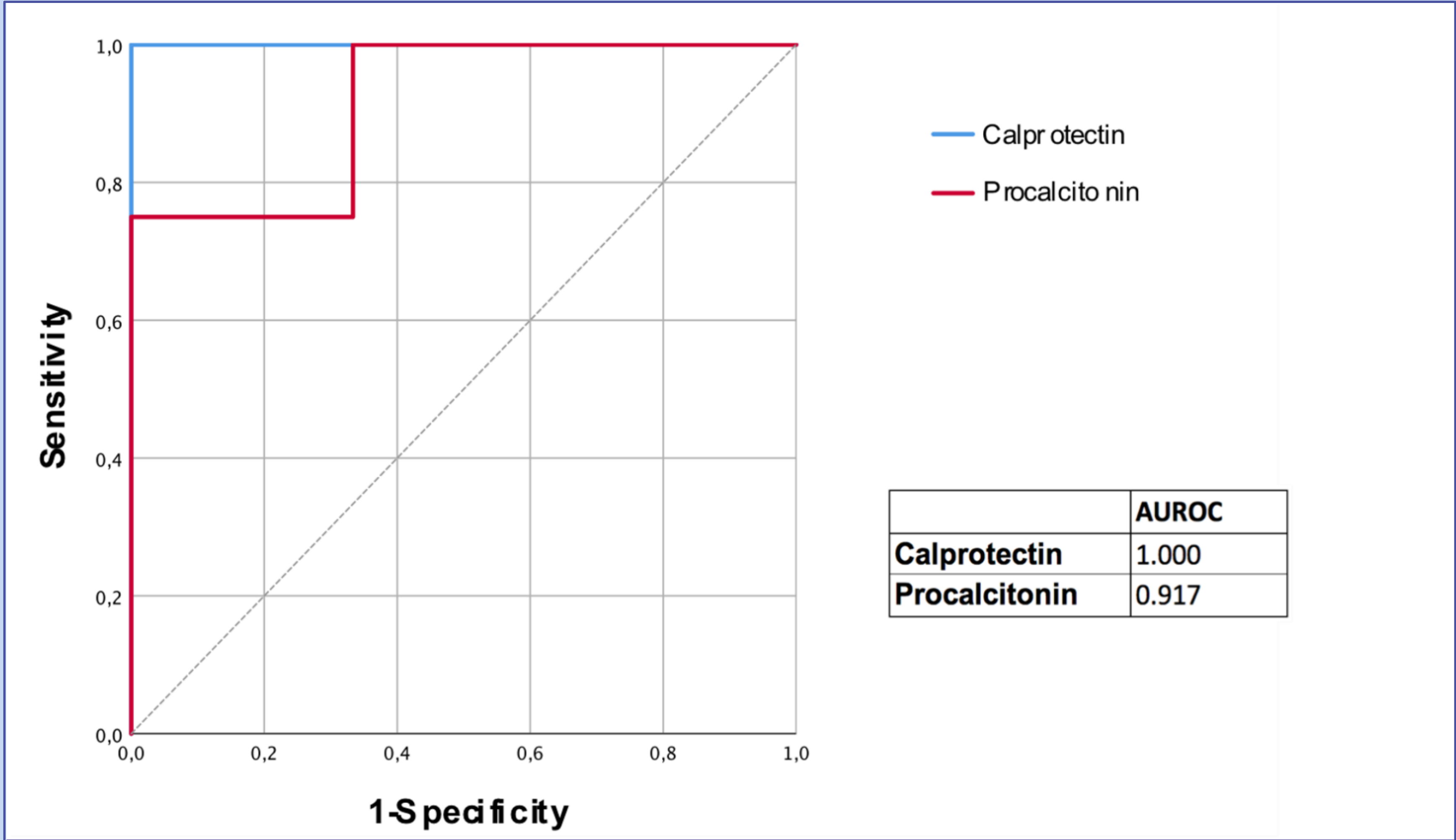
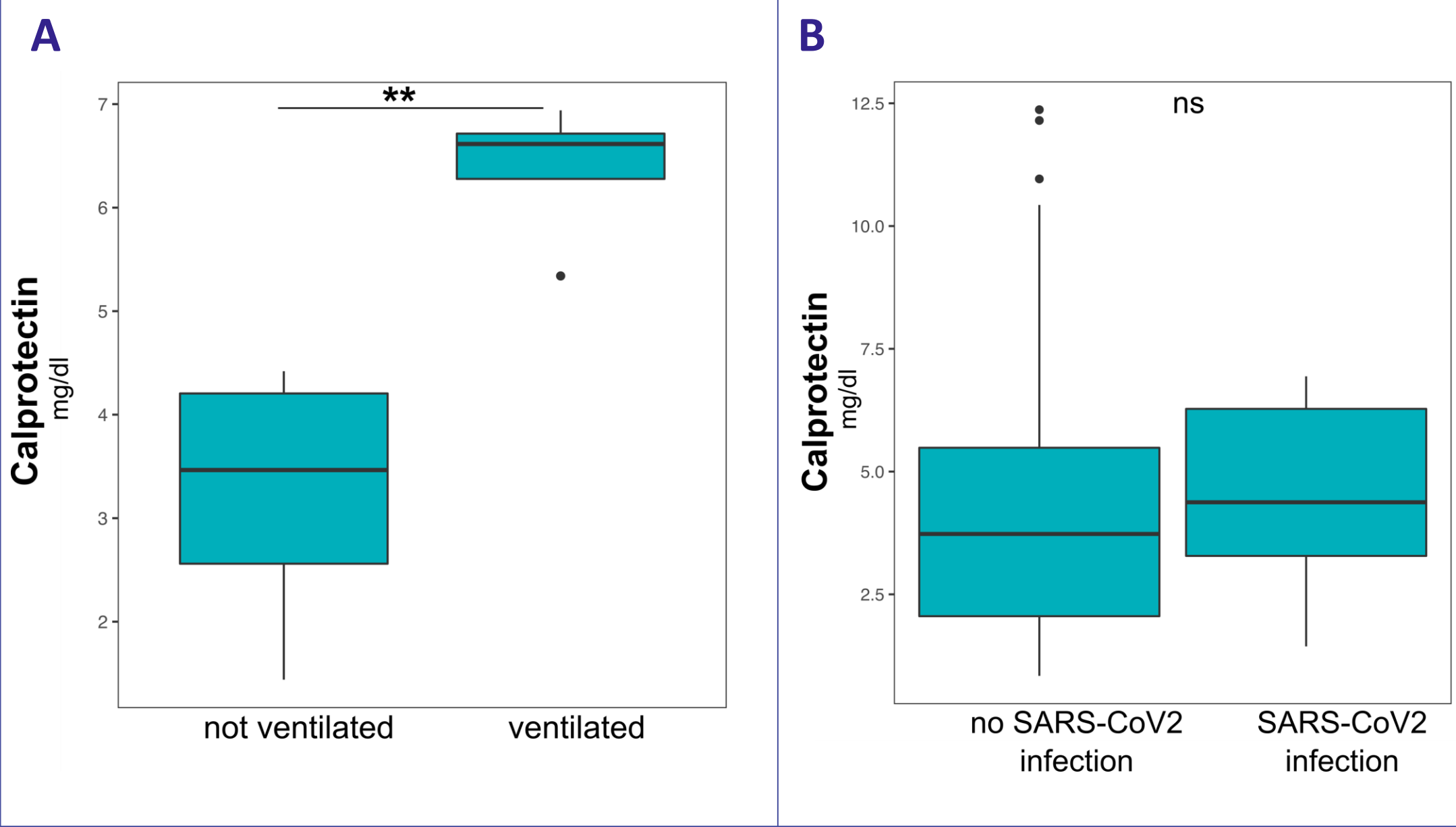
Results:

A total of 4 out of 10 COVID-19 patients were admitted to ICU and 1 patient died. Age median was 67 years (standard deviation 17.6 years) with 54% being male patients, in COVID-19 group of patients the median age was 48 (standard deviation 14.8 years) with 80% male patients. Calprotectin was measured in heparin plasma by PETIA method from Gentian AS, Norway. It was significantly higher in ventilated than in non-ventilated COVID-19 patients. Calprotectin was able to predict ICU-admission with an AUROC of 1.0 and performed better than procalcitonin.

|                                       | N  | Overall          | SARS-CoV2         | Non SARS-CoV2    | P-value |
|---------------------------------------|----|------------------|-------------------|------------------|---------|
| Number of patients [n (%)]            | 70 | 70 (100)         | 10 (14,3)         | 60 (85,7)        |         |
| Demographics                          |    |                  |                   |                  |         |
| Age [Mean (IQR)]                      | 70 | 67 (51-78)       | 48 (41-60)        | 70 (53-80)       | 0,012   |
| Sex female [n (%)]                    | 70 | 31 (44,3)        | 2 (20)            | 29 (48,3)        | 0,097   |
| Vital signs                           |    |                  |                   |                  |         |
| BP syst. (mmHg) [Mean (IQR)]          | 70 | 135 (116-140)    | 133 (116-140)     | 137 (116-154)    | 0,557   |
| Respiration rate (/min.) [Mean (IQR)] | 70 | 16 (14-22)       | 18 (15-25)        | 16 (14-21)       | 0,385   |
| Laboratory data                       |    |                  |                   |                  |         |
| Creatinine (mg/dl) [Mean (IQR)]       | 70 | 0,94 (0,76-1,29) | 0,93 (0,78-1)     | 0,94 (0,75-1,31) | 0,808   |
| Bilirubin (mg/dl) [Mean (IQR)]        | 55 | 0,59 (0,32-0,94) | 0,6 (0,37-0,74)   | 0,58 (0,32-0,95) | 0,904   |
| Procalcitonin [µg/l] [Mean (IQR)]     | 49 | 0,17 (0,08-0,62) | 0,1 (0,7-0,31)    | 0,18 (0,08-0,68) | 0,275   |
| CRP [mg/l] [Mean (IQR)]               | 64 | 27,2 (1,9-114,5) | 70,3 (21,3-152,8) | 15,9 (1,4-106,9) | 0,144   |
| WBC (/nl) [Mean (IQR)]                | 70 | 7,8 (4,5-12,7)   | 7,3 (6,2-8,1)     | 8,3 (3,5-12,9)   | 0,397   |
| Platelets (/nl) [Mean (IQR)]          | 70 | 226 (174-285)    | 163 (152-211)     | 235 (192-290)    | 0,006   |
| ICU admission [n (%)]                 | 69 | 11 (15,7)        | 4 (40)            | 7 (11,7)         | 0,026   |
| Mechanical ventilation [n (%)]        | 69 | 8 (11,4)         | 4 (40)            | 4 (6,7)          | 0,003   |
| Comorbidities [n (%)]                 | 70 | 58 (82,9)        | 7 (70)            | 51 (85)          | 0,247   |
| 90-days mortality [n (%)]             | 70 | 6 (8,6)          | 1 (10)            | 5 (8,3)          | 0,863   |

**Tab. 1:** Baseline characteristics of the recruited patients until May 2021. IQR = interquartile range; BP syst. = systolic blood pressure

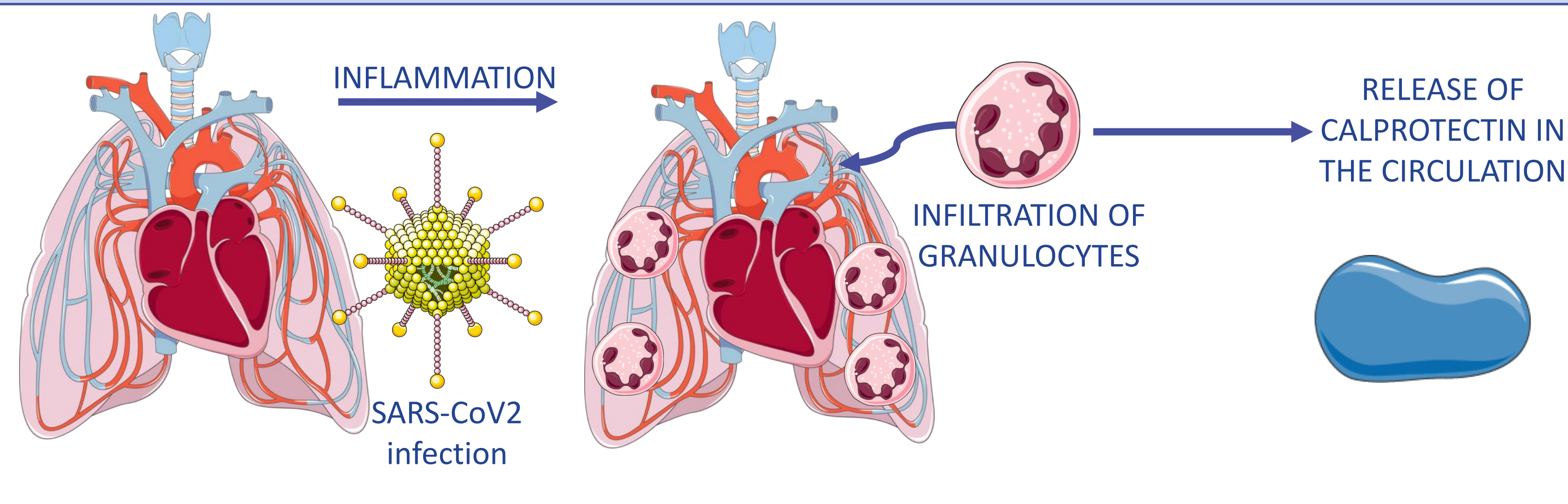
**Fig.2:** Calprotectin levels in COVID-19 (ventilated and non-ventilated) and infectious, non-COVID-19 ICU patients.  
A ventilated = 4, not ventilated = 6;  
B infectious non-COVID n = 60, COVID = 10;  
\*\* = p < 0.01, ns = non significant



**Fig. 3:** Receiver operating curve for Calprotectin and Procalcitonin predicting Intensive Care Unit (ICU) admission in COVID patients. Calprotectin is outperforming Procalcitonin in the preliminary cohort in predicting admission to the ICU. n = 10

Conclusion and perspective:

Calprotectin is an easy to assess blood biomarker that is able to predict severe courses of disease in COVID-19 patients presented at the ED. The reason for this might be that especially the lung injury that is caused by macrophages and granulocytes is associated with poor outcome<sup>3</sup>. Macrophages and granulocytes release calprotectin which is highly involved in the pro-inflammatory response generated in COVID-19.



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References:

<sup>1</sup>Kotsiou, O. S., et al.. Calprotectin in Lung Diseases. IJMS 22, 1706 (2021).  
<sup>2</sup>Bauer, W. et al. Outcome prediction by serum calprotectin in patients with COVID-19 in the emergency department. J Infect 82, 84–123 (2021).  
<sup>3</sup>Rendeiro, A. F. et al. The spatial landscape of lung pathology during COVID-19 progression. Nature 593, 564–569 (2021).