Introduction:
Heterotopic ossification (HO) is the formation of bone in soft tissues and constitutes a potential complication of patients hospitalized in the ICU. The exact pathogenetic mechanisms of HO are unknown. Bone morphogenic proteins (BMPs) induce bone formation, while signaling through the receptor activator of NF-κB (RANK) and its ligand (RANKL) regulates osteoclast formation, activation and survival in normal bone modeling and remodeling. Osteoprotegerin (OPG) protects bone from excessive bone loss by preventing RANKL from binding to RANK. In the present study we investigated these molecules as possible biomarkers of HO development in ICU patients.

Methods:
We measured the levels of BMP-2, RANKL and OPG on ICU admission, and thereafter on days 7 and 30 in the sera of 28 critically ill patients using ELISA.

Results:
Nine of the 28 patients developed HO in the ICU or during the 30-day follow-up period. Our results showed that on admission to the ICU, the patients who developed HO had significantly lower BMP-2 levels compared to patients who didn’t [566.7 (216.7-883.3) pg/ml vs. 1300 (566.7-2817) pg/ml, respectively, p= 0.037]. RANKL levels were also decreased in the HO patients on admission [1.495 (0.285-2.465) ng/ml vs. 2.465 (1.535-6.67) ng/ml, p= 0.048], while OPG levels were similar in both groups. In the HO patients, on day 7, the levels of BMP-2 were slightly elevated, whereas on day 30 they tended to increase (p= 0.064). The patients who did not develop HO had stably elevated levels during the 30 days. A small elevation was noted in RANKL levels in the HO patients, while OPG levels remained unaltered at all time points, for both groups.

Conclusion:
In our cohort of critically ill patients, those who will develop heterotopic ossification have significantly decreased levels of BMP-2 and RANKL on admission, suggesting that these molecules may be used as prognostic markers to identify patients who will develop this debilitating condition.