

Splenectomy improves functional outcome of experimental intracerebral haemorrhage (ICH) in mouse models through increased haematoma resorption



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INTRODUCTION

ICH is a type of stroke that involves bleeding within the brain parenchyma. The peripheral immune system, particularly the spleen, plays a role in damage caused by ICH¹. Splenectomy has been shown to reduce inflammation and improve functional outcome in ischaemic stroke². However, the effect of splenectomy on ICH has not been studied. This study investigated the effect of splenectomy on functional outcomes of ICH and the molecular mechanism behind.

METHODS

The effect of splenectomy on the functional outcome of ICH was demonstrated in mouse models. Splenectomy was performed 2 weeks before inducing ICH. The spleen is removed by cauterising the vessels. ICH was induced in 12-week old C57/6J mice fed with normal diet, by intrastriatal injection of type IV collagenase³. The mouse models were separated into two groups: ICH mice which had undergone splenectomy and ICH mice which had undergone laparotomy. The percentage survival of mouse models, neurofunctional assessment results, haematoma size and volume were measured throughout the investigation.

RESULTS

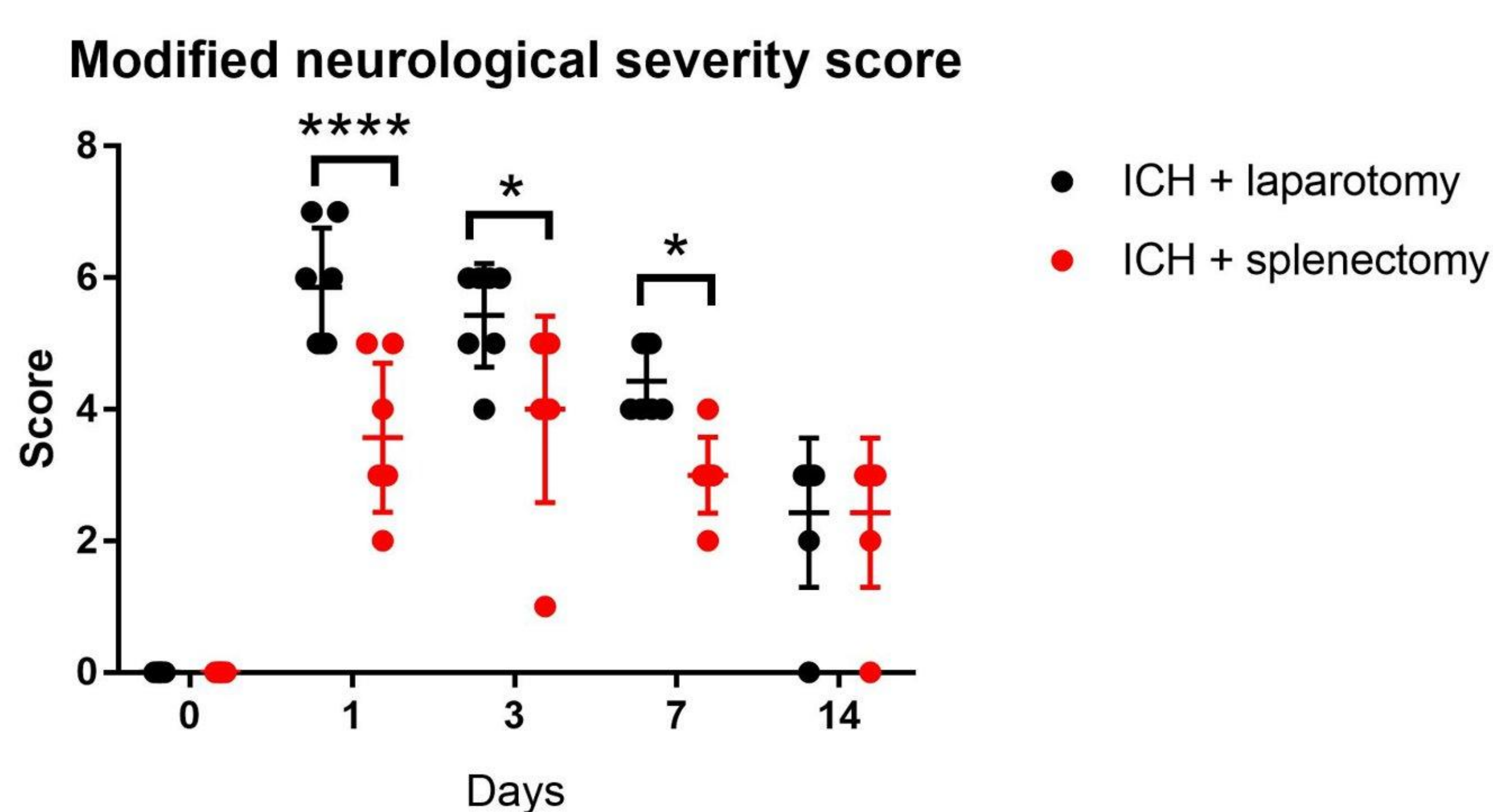


Figure 1a: Modified neurological severity score (mNSS) of mouse models on days 0 (pre-ICH baseline), 1, 3, 7 and 14. A higher mNSS indicates a more severe stroke condition and worse motor functions.

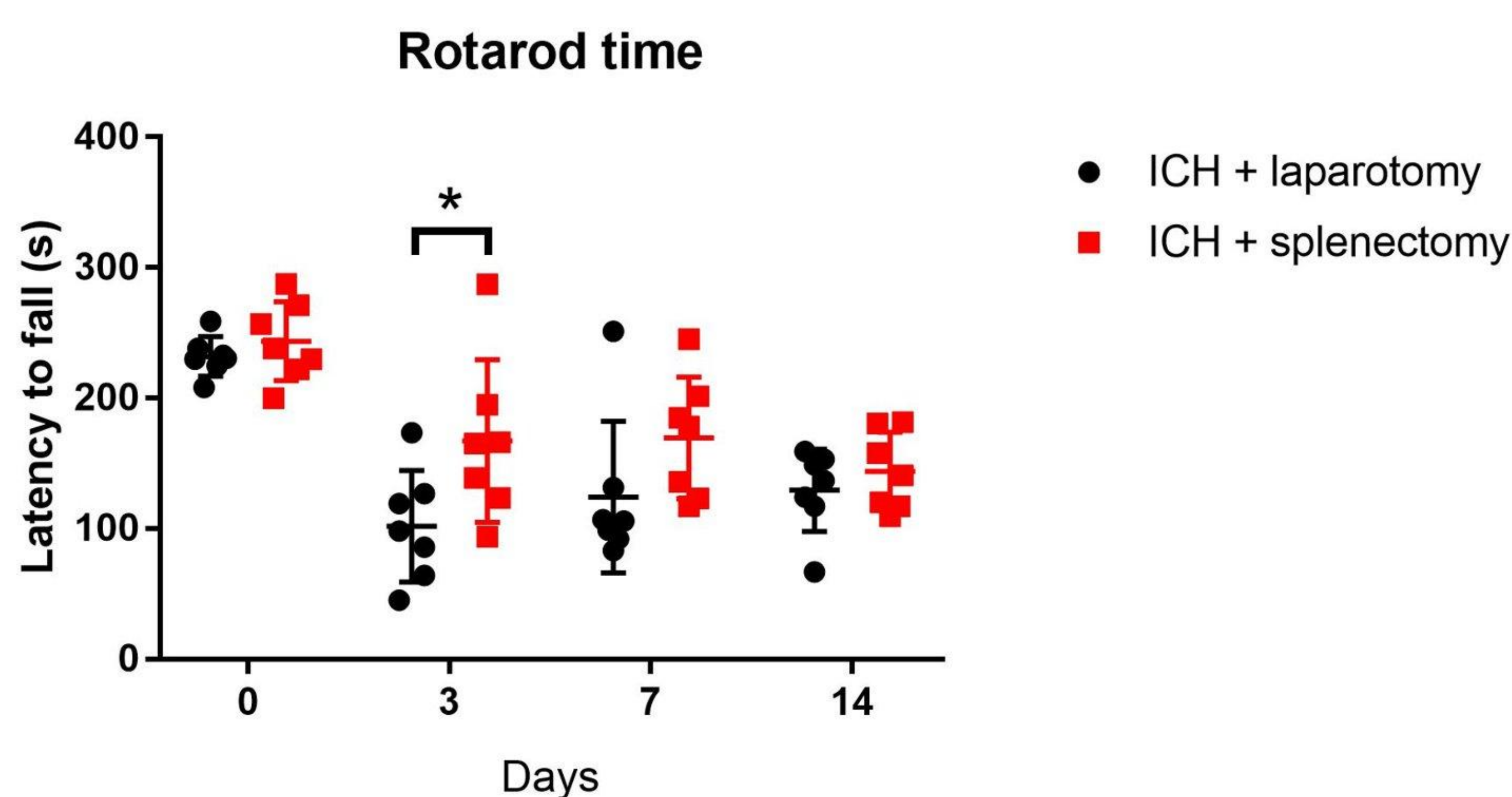


Figure 1b: Rotarod test results of mouse models on days 0 (pre-ICH baseline), 3, 7 and 14. The length of time they can stay on the Rotarod is recorded. A shorter duration indicates worse motor function hence worse recovery.

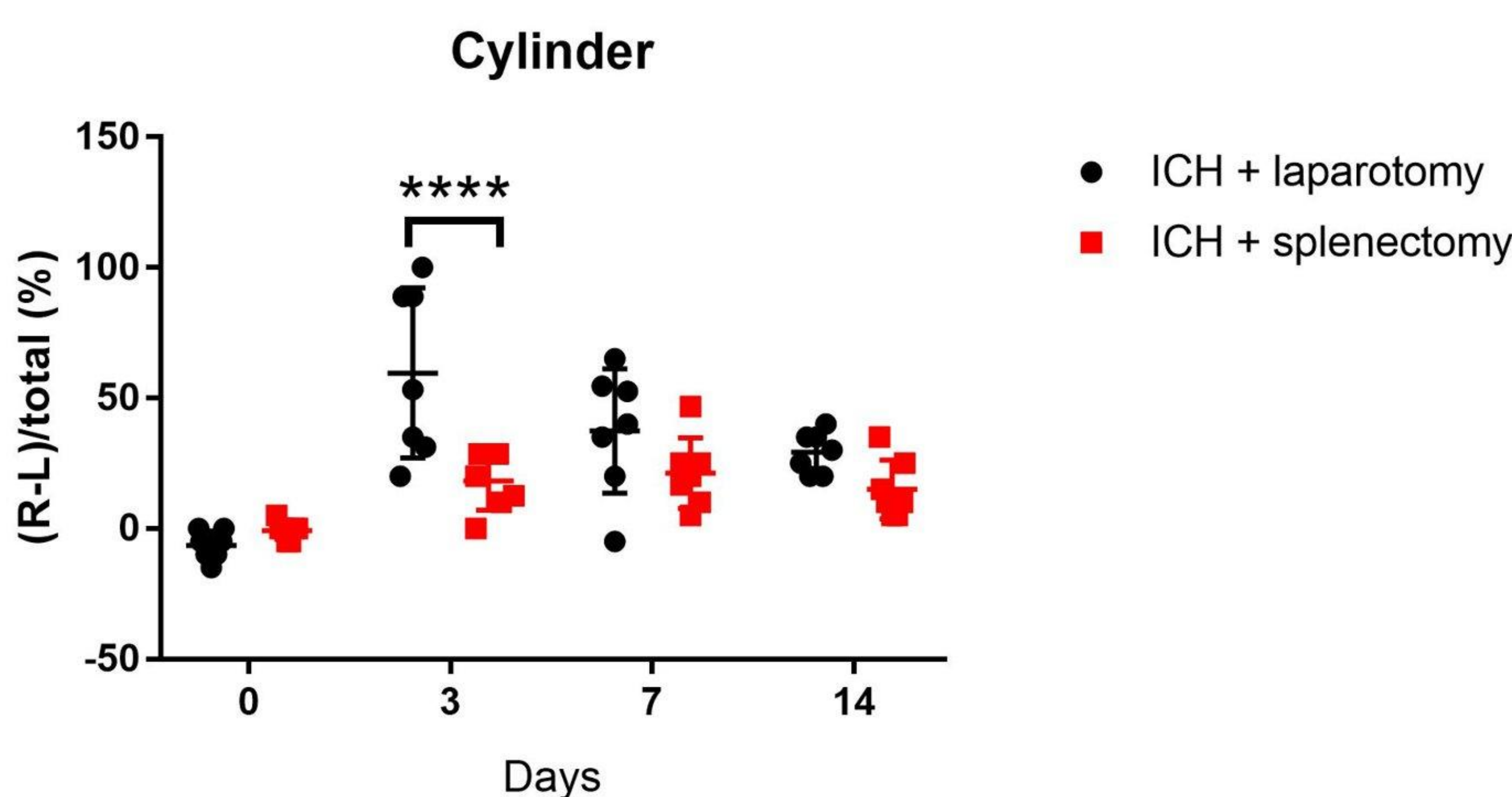


Figure 1c: Cylinder test results of mouse models on days 0 (pre-ICH baseline), 3, 7 and 14. The laterality index is measured. A higher laterality index indicates higher lateralisation hence worse recovery.

Mice that had undergone splenectomy 2 weeks before ICH showed better functional outcomes than those with laparotomy. The modified Neurological Severity Scores (mNSS) were significantly improved on day 1 ($p < 0.0001$), day 3 ($p = 0.0192$) and day 7 ($p = 0.0192$). We also demonstrated improved Rotarod test ($p = 0.0227$) and cylinder test ($p < 0.0001$) results on day 3.

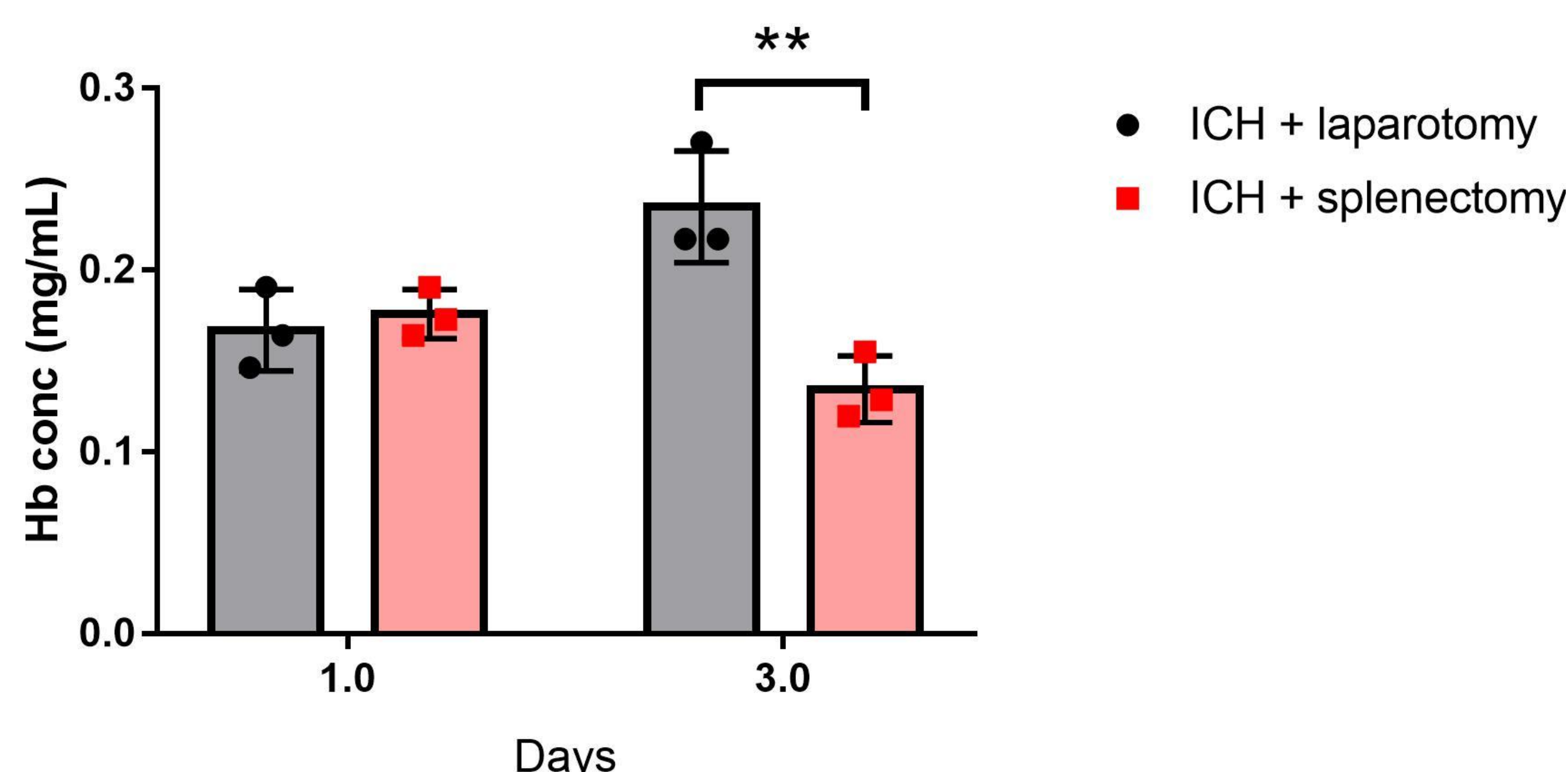


Figure 2a: Haemoglobin concentrations of mouse brain samples on days 1 and 3. Drabkin's reagent is used in this haemoglobin assay.

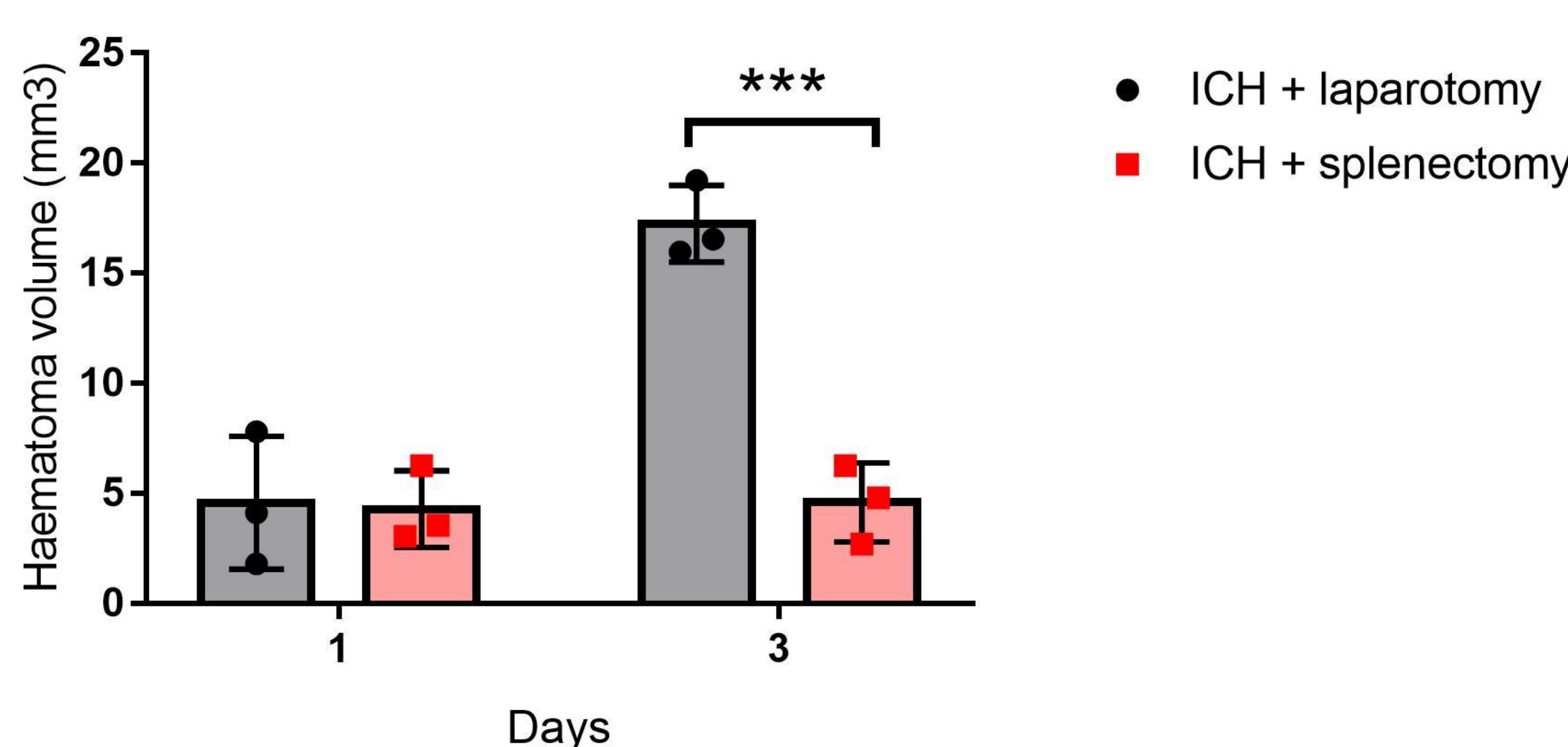


Figure 2b: Haematoma volumes of mouse brain samples on days 1 and 3. Haematoma volumes are quantified based on the digital analysis of consecutive brain sections

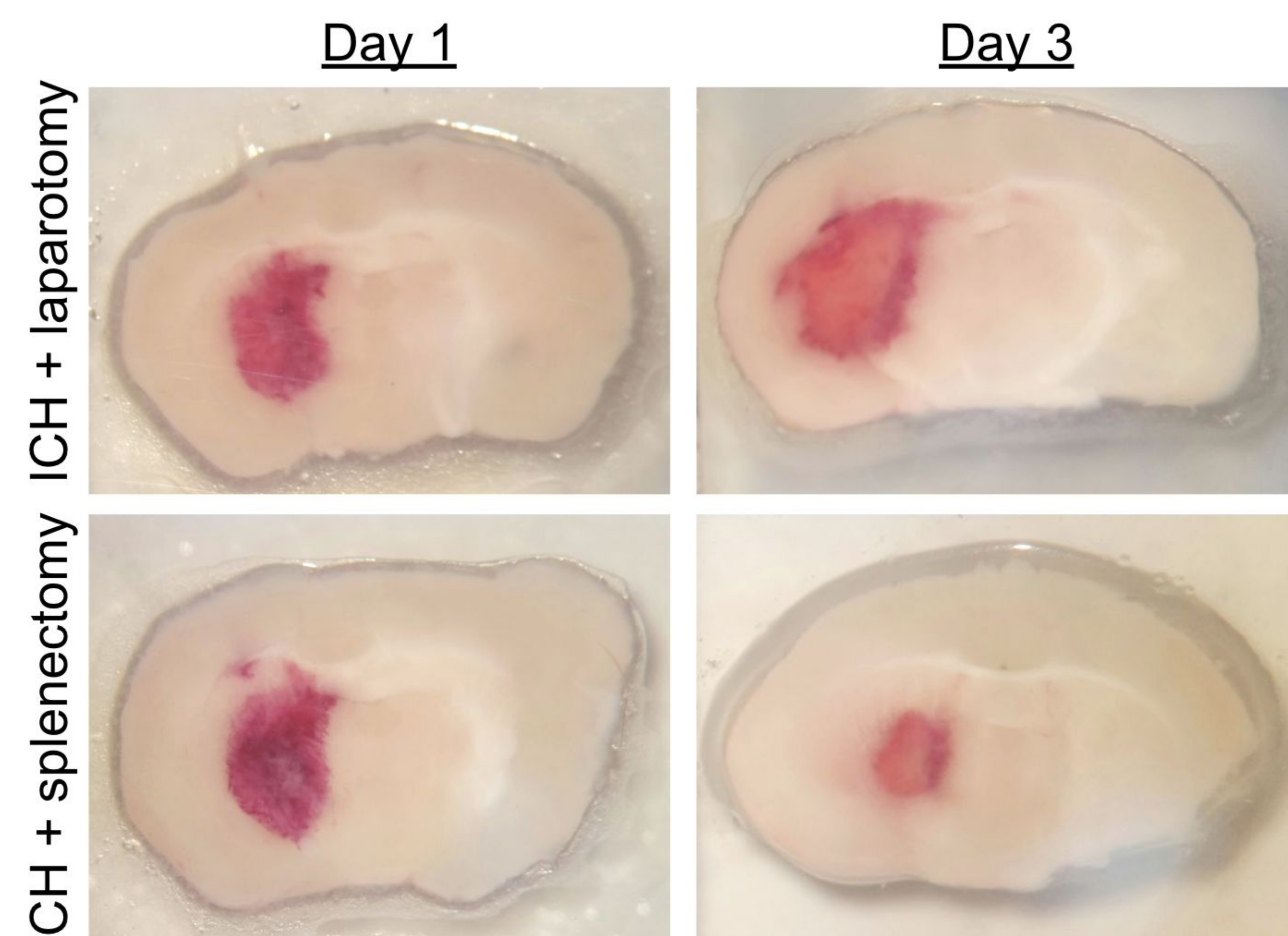


Figure 2c: Haematoma sizes of mouse brain samples on days 1 and 3.

Mice that had undergone splenectomy 2 weeks before ICH showed similar haemoglobin concentrations and haematoma volumes on day 1 when compared to those with laparotomy only. However, the splenectomised group showed a lower haemoglobin concentration ($p = 0.0011$) and smaller haematoma volume ($p = 0.0002$) on day 3. These data suggest that splenectomy facilitates haematoma resorption, resulting in improved functional outcome.

CONCLUSION

Splenectomy 2 weeks before ICH improves functional outcome of experimental ICH through increased haematoma resorption.

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