

Study on measurement of internal anal sphincter (IAS) movement in dogs (application as evaluation method on defecation disorder) -the 3rd report

○ Kazuaki Sasaki, Yasuyuki Ootsuka, Hirohiko Akahoshi, Kousuke Morizumi, Seiichi Katayama, Katsuhide Nishi

Objective

The number of potential fecal incontinence patient in Japan is estimated to be about 5 million, but no fundamental treatment has been developed so far. Therefore, development of new treatments and/or novel drugs is expected. Screening using animal models is important for development of new therapeutic agents. In the present study, we developed a method for measuring the internal and sphincter (IAS) contractile activity in dogs under sedation. The dog fecal incontinence model was created by impairing IAS. The contractile activity was measured by manometry using a pressure sensor catheter. By periodically measuring the IAS contractile activity before and after the model creation in this model, we obtained basic data of the contractile activity during the process of spontaneous healing, and we also investigated the effects of a comparative control substance, phenylephrine, aimed for the future evaluation of the efficacy of new drugs.

Materials and Methods

Animal

Beagle dog, 6 males, 17-32 month-old

Preparation of dog fecal incontinence model

Under anesthesia, the internal anal sphincter was dissected, cauterized with an electric scalpel, and crushed with forceps to damage the muscle tissue and reducing its contractile function. The upper and lower parts (approximately 2x2 cm) of the internal anal sphincter were targeted to dissect, cauterize and crush.

Equipment

Equipment	Model	Manufacturer
Millar Mikro-Tip Catheter	MPR-500	Millar
Transducer control unit	TCB-510	Millar
Power Lab	ML846	ADInstruments
Data analysis software	Lab Chart Pro	ADInstruments
Automatic extraction device	Pro filometer 1725	Life-Tec Inc.

Experimental design

Saline (N=6), 5 mL/body, Rectal administration

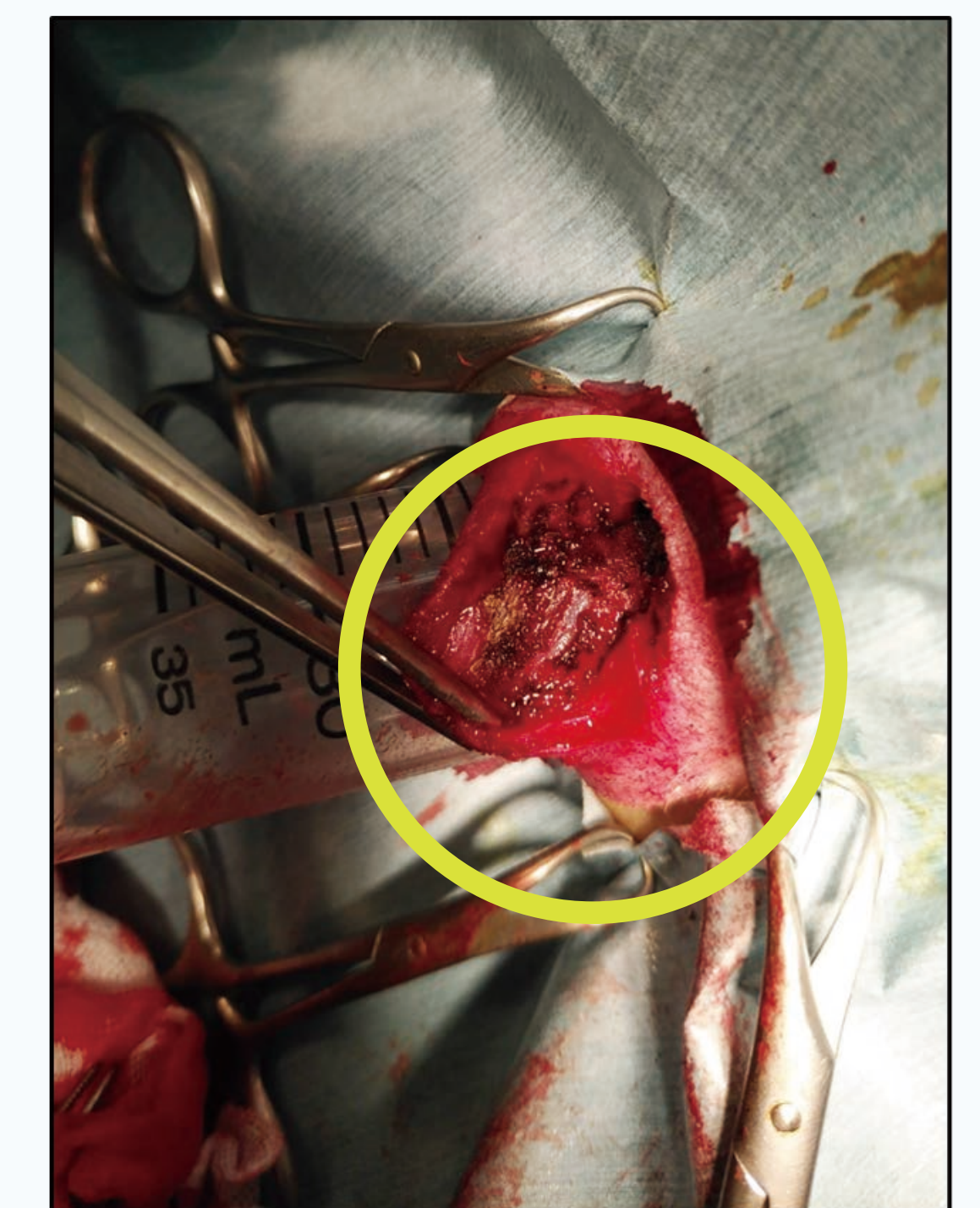
Phenylephrine 0.5 mg/body (N=6), 5 mL/body, Rectal administration

Evaluation Items

Area (mmHg·15sec), and Peak (mmHg·15sec) of Internal anal sphincter contraction waveform

Summary in Japanese

わが国の便失禁の潜在患者数はおよそ500万人程度になると推定されているが、現状、根本的な治療法は開発されておらず、新たな治療法及び治療薬の開発が望まれている。新たな治療薬の開発には、モデル動物を用いたスクリーニングが重要である。そこで我々はフォーストランスデューサーを内肛門括約筋に留置し、収縮運動をテレメトリー方式で取得する方法により、無麻酔無拘束下のイヌを用いた内肛門括約筋収縮運動測定法を立ち上げ、第91回及び第92回日本薬理学会年会で発表した。今回我々は、内肛門括約筋に障害を負わせることで排便障害モデルを作製し、圧センサーカテーテルを用いたマンOMETRY法にて内肛門括約筋の収縮運動を測定し、鎮静下でのイヌを用いて内肛門括約筋収縮運動測定法を立ち上げた。モデル作成前及び作成後の内肛門括約筋収縮運動を定期的に測定することで、自然治癒の過程での内肛門括約筋収縮運動を測定し基礎データを取得した。また、薬物の作用を評価するにあたり、比較対照物質(フェニレフリン塩酸塩)の検討も実施したので報告する。



The dog fecal incontinence model was created by impairing IAS.

Study schedule



Results

Fig. 1 Effects of phenylephrine on contraction response of IAS before surgery

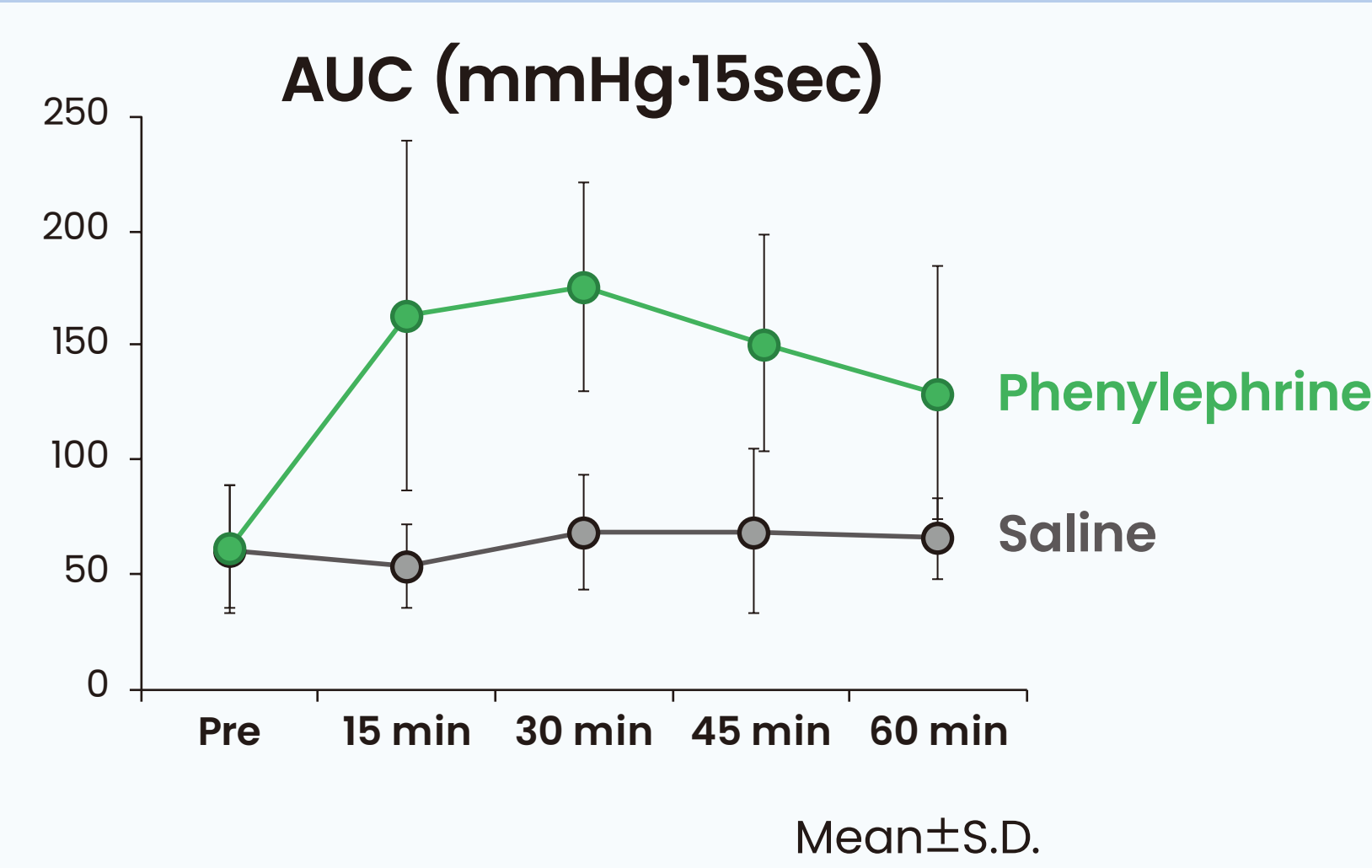


Fig. 2 The % changes over time of IAS during the period of 5 weeks after surgery

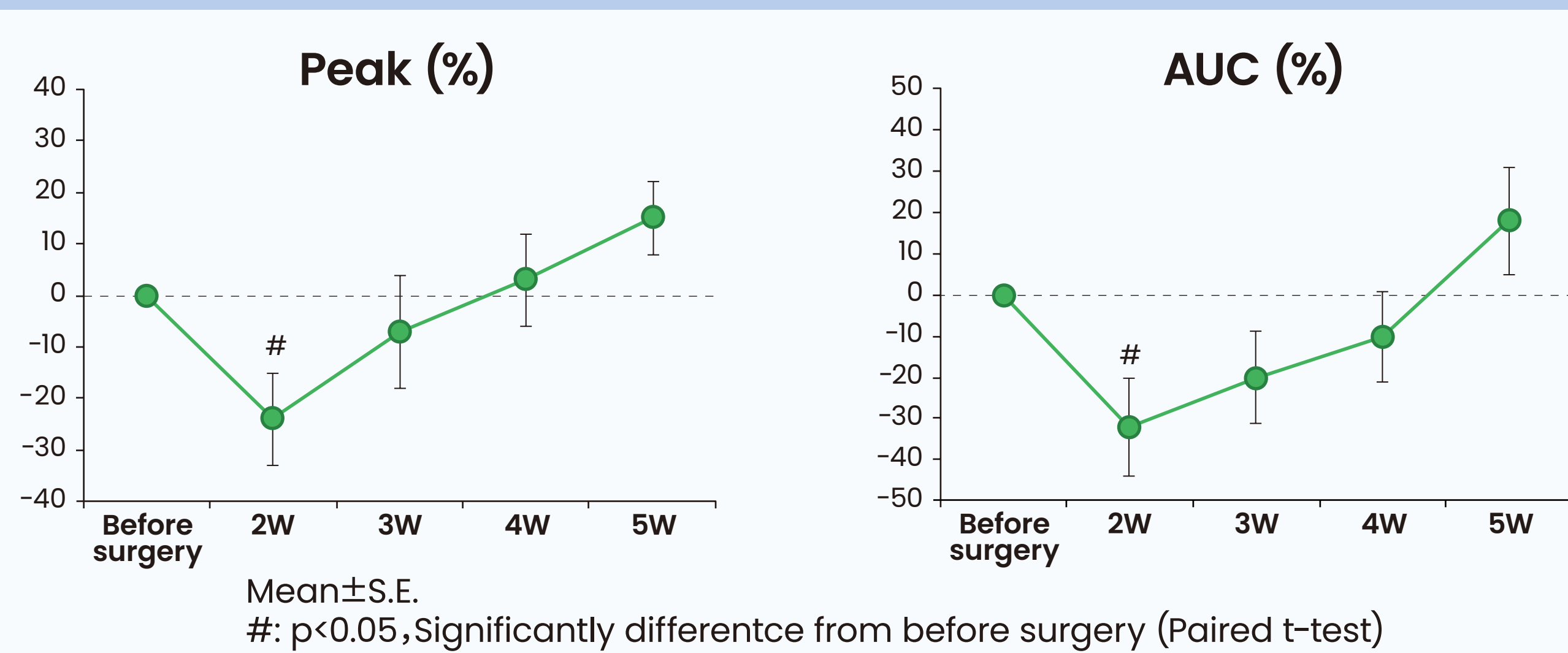


Fig. 3 Typical waveform of IAS during administration of phenylephrine

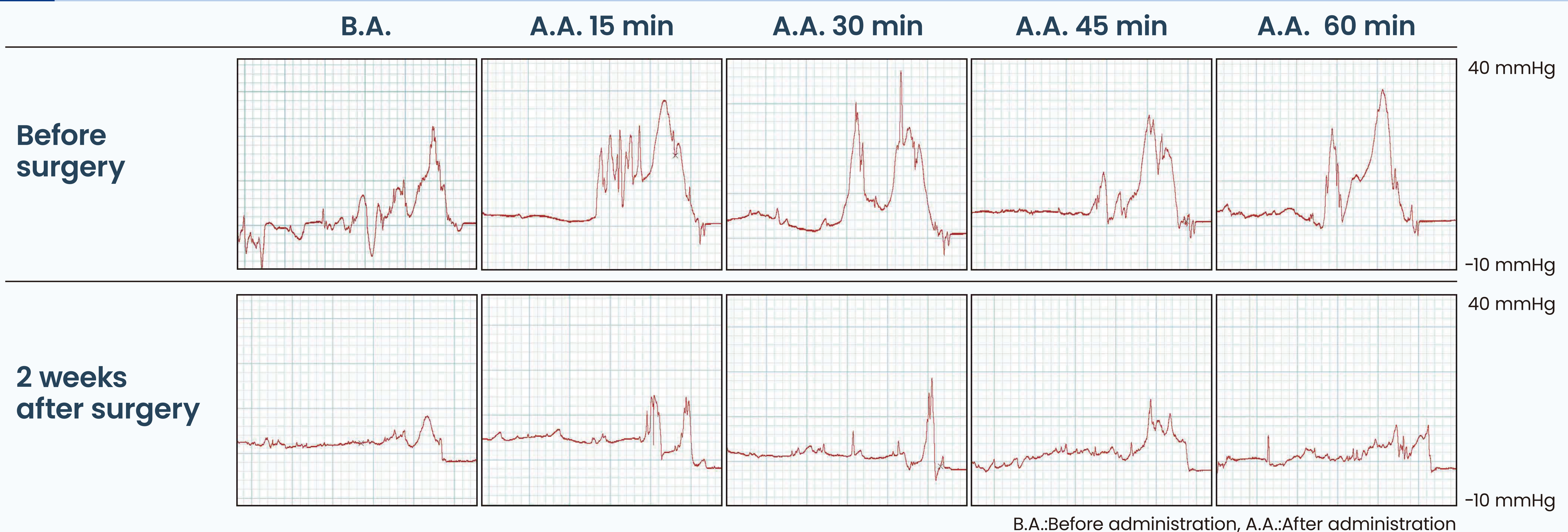
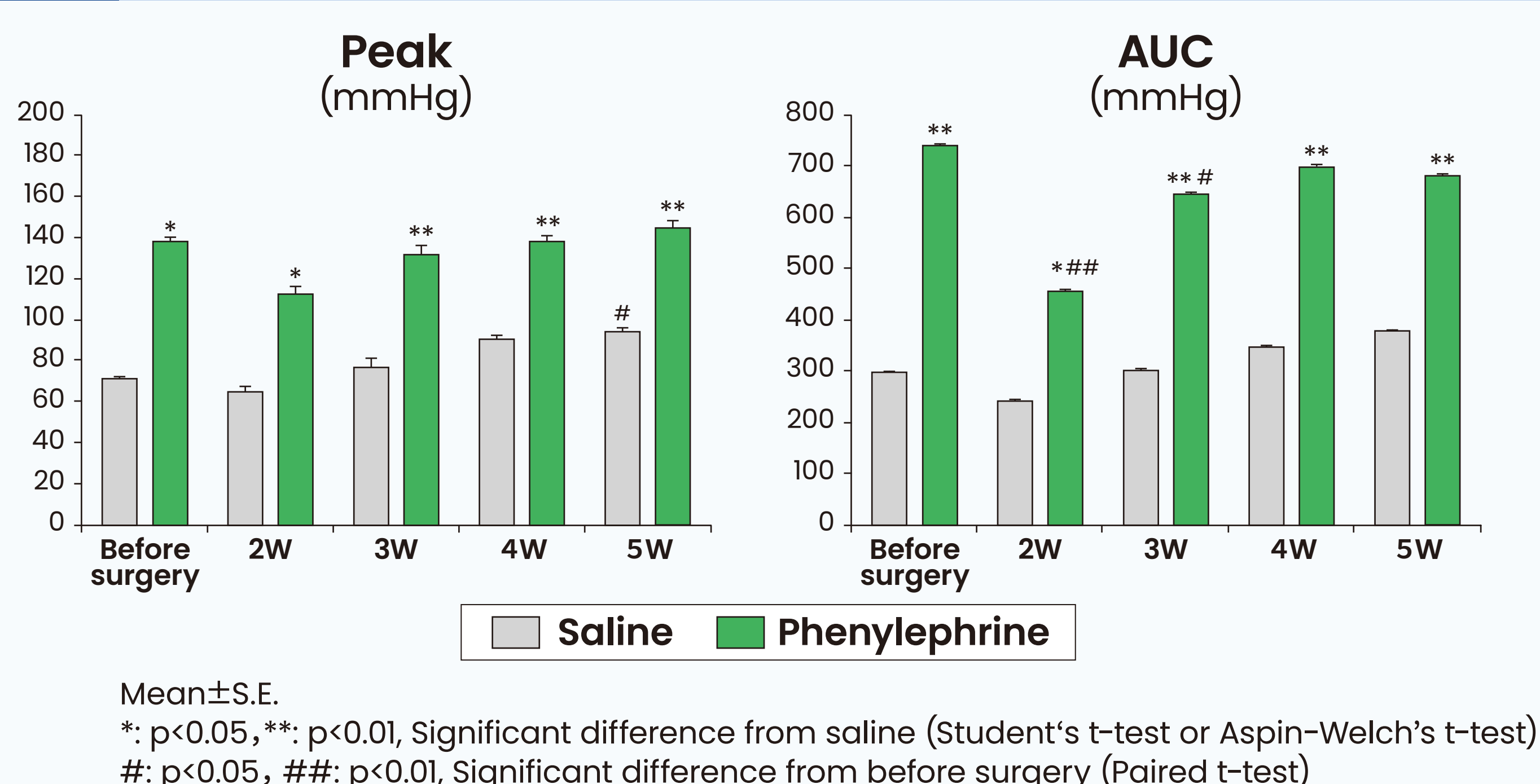


Fig. 4 Accumulated value for 15-60 minutes



Conclusion

Using an animal model of fecal incontinence in which the internal anal sphincter was injured, the contractile force of the internal anal sphincter was measured up to 5 weeks after surgery.

The contractile force of the internal anal sphincter muscle significantly decreased at two weeks after surgery and then gradually recovered up to 5 weeks (Fig. 2).

Phenylephrine administration consistently increased the contractile force from before surgery to 5 weeks after surgery compared to the control group, though the force significantly decreased two weeks after surgery compared to before surgery (Fig. 4).

Based on these results, it is suggested that this model can be used to evaluate the contraction response of the internal anal sphincter in dogs.