Direct Oral Anticoagulants
Use in the Setting of Bariatric Surgery and Feeding Tubes

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### DOAC Absorption

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Absorption Location</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Apixaban</td>
<td>Primarily small intestine with some gastric absorption and pH independent absorption in proximal colon*</td>
<td>pH independent absorption</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>Lower stomach and duodenum</td>
<td>Prodrug requires acidic environment for absorption (formulated with tartaric acid)</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Primarily small intestine</td>
<td>pH dependent solubility</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Primarily stomach with reduced absorption in the proximal and small intestine</td>
<td>20mg and 15mg tablets must be taken with a sufficient caloric intake; following bariatric surgery, most patients must adhere to a caloric restriction</td>
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### Bariatric Surgery

**Types of Bariatric Surgery**

- **Adjustable gastric banding (AGB):** Adjustable silicone band placed around stomach to create a smaller pouch.
- **Roux-en-Y gastric bypass (RYGB):** Stomach stapled to form gastric pouch that connects to distal jejunum, excluding the duodenum and proximal jejunum.
- **Gastrectomy (partial/sleeve):** Sleeve gastrectomy results in longitudinal resection of 80% of stomach.
- **Colecctomy:** Surgical removal of all or part of the colon. (visual not provided)

### Potential impact of surgical intervention on absorption

<table>
<thead>
<tr>
<th>Apixaban</th>
<th>Dabigatran</th>
<th>Edoxaban</th>
<th>Rivaroxaban</th>
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### Feeding Tubes

- **Apixaban:** Bioavailability is also reduced if administered distal to the stomach. It is recommended to avoid in conjunction with food. Can be given in 60ml of D5W. Flushing tube should not be administered if terminated in the stomach (nasogastric or gastric tubes).
- **Edoxaban:** No studies have been conducted to assess edoxaban use in enteral administration therefore it should be taken as an intact tablet.
- **Rivaroxaban:** Bioavailability is reduced if administered distal to the stomach. It is recommended to flush tubing prior to and after administration. Can be given in 50ml of sterile water, applesauce, or juice.
- **Dabigatran:** Must be taken orally and should not be administered through an enteral feeding tube.

### Take Home Points

- There is minimal evidence regarding the use of DOACs in patients with a history of bariatric surgery. 2021 ISTH guidelines specifically address DOAC use following bariatric surgery for treatment/prevention of VTE and recommend treatment with a parenteral anticoagulant in the early/acute setting, followed by a switch to VKA or DOAC in the stable post-acute phase.
- Rivaroxaban should be used with extra caution due to the caloric restrictions associated with gastric bypass, as well as reduction in plasma levels as seen in observational studies.
- If a patient is unable or unwilling to use warfarin, it is important to consider type of bariatric surgery, location of DOAC absorption, pH dependent/independent solubility, transporter mechanisms and to conduct shared decision making prior to initiating DOAC therapy.
- Dabigatran and edoxaban are not recommended for administration via enteral feeding tubes. Rivaroxaban and apixaban can be administered via enteral feeding tubes if terminated in the stomach (nasogastric or gastric tubes).

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### Notes

- Bariatric surgery results in weight loss by reducing stomach volume (which results in a more alkaline pH) and/or reducing effective intestinal surface area which results in malabsorption.
- ALL DOACs are substrates of P-gp. Apixaban and rivaroxaban are substrates of CYP3A4.
- Pgp concentration is lowest in the duodenum and highest in the distal ileum and colon. Bypassing the proximal portions of the GIT (RYGB) could lead to decreased drug absorption due to increased efflux of DOAC back into the gut lumen.
- CYP3A4 is located along the entire small intestine with slightly increased expression from the duodenum to the middle section of the jejunum with gradually reduced expression in the distal jejunum and ileum. Bypassing the proximal segments (RYGB) of the GIT could result in a significant increase in oral bioavailability of substrates due to decreased metabolism.

### References