Estratégias Clínicas para Controlar Hemorragias Gastrointestinais Agudas e Anemia sem Transfusão de Sangue*

PRINCÍPIOS GERAIS DE TRATAMENTO

1. **Formular um plano de controle clínico abrangente** para facilitar uma tomada de decisão rápida e evitar demoras no tratamento, incluindo uma combinação de modalidades de conservação de sangue**.**
2. Exercendo bom senso clínico, **estar preparado para modificar práticas de rotina** (p. ex., interrupção rápida e agressiva do sangramento, tolerância de hipotensão moderada durante o sangramento descontrolado).
3. **Considerar os procedimentos previstos ou de uso potencial,** bem como seus riscos e benefícios, com o paciente ou com o seu substituto para tomar decisões.
4. **Certificar-se da disponibilidade de pessoal bem treinado, experiente,** e de medicamentos e equipamentos necessários para prevenção e controle rápido de hemorragias.
5. **Adotar um enfoque de equipe interdisciplinar e colaborador** entre as especialidades envolvidas (gastroenterologia, medicina interna, radiologia, cirurgia, anestesiologia, terapia intensiva, hematologia) sob a direção ativa do clínico chefe.
6. **Manter comunicação contínua** sobre o tratamento do paciente. Caso haja múltiplos quadros clínicos tratados por vários médicos, é de suma importância a colaboração e a coordenação entre as especialidades.
7. **Consultar imediatamente especialistas** experientes em tratar pacientes sem transfusão de sangue alogênico. O reconhecimento dos fatores de risco de sangramento ou anemia pode ajudar os médicos a predizer/antecipar a necessidade de medidas preventivas ou de controle.
8. **Manter vigilância contínua e rigorosa para identificar sinais e sintomas de perda de sangue** ou de deterioração do quadro clínico. Estabelecer um limiar mais baixo para pronta intervenção, no caso dos pacientes que não consideram como opção a transfusão de sangue alogênico.
9. **Interrupção imediata da perda de sangue e um controle criterioso do volume pode salvar vidas.** No paciente com sangramento ativo e que não pode ser transfundido, não se deve considerar como uma opção esperar que o sangramento gastrointestinal (GI) diminua espontaneamente. Deve-se procurar tirar o máximo benefício possível de todo o tratamento disponível para reduzir a perda de sangue e manter a perfusão. Em caso de hemorragia grave, é de suma importância recorrer imediatamente a medidas definitivas para controlar e parar o sangramento.
10. Se necessário, **transferir** para um centro maior o paciente estável, **antes que o seu estado se agrave.**

PRINCÍPIOS TERAPÊUTICOS GERAIS

1. Criteriosa ressuscitação com fluidos. Na presença de hemorragia descontrolada, considere aceitável uma hipotensão moderada e uma ressuscitação controlada com fluidos para não agravar um sangramento que esteja em processo, até que o mesmo seja prontamente interrompido. No paciente anêmico, depois que a hemorragia for controlada, mantenha a normovolemia.
2. Histórico médico, exame físico, medidas de ressuscitação, procedimentos de diagnóstico, lavagem, etc., são procedimentos dinâmicos que podem ser realizados a um só tempo.
3. Diagnóstico rápido, pronta localização e interrupção da hemorragia, bem como prever e realizar profilaxia contra hemorragia recorrente são de suma importância para o controle de um sangramento GI agudo sem usar transfusão de sangue.
4. Usar as intervenções diagnósticas disponíveis que possam localizar a(s) fonte(s) do sangramento com maior rapidez.
5. Interromper prontamente um sangramento ativo por instituir, de imediato, a terapia específica por endoscopistas ou cirurgiões bem treinados e habilidosos.
6. Usar agentes farmacológicos para suprimir a produção do ácido gástrico, melhorar a condição de coagulação e promover a hemostasia.

SUMÁRIO — *PÁGINA*

* Nota: Estas informações são dirigidas aos gastroenterologistas, médicos que fazem o primeiro atendimento, cirurgiões, anestesiologistas, hematologistas e outros especialistas como um documento útil e de referência acessível. As opções de procedimentos apresentadas aqui não descrevem um método exclusivo de tratamento. **Talvez nem todas as estratégias alistadas sejam apropriadas ou aceitáveis para todos os pacientes.** Ao mesmo tempo em que respeitam a vontade do paciente, os médicos devem fazer uma análise clínica criteriosa, consultar especialistas mais experientes e individualizar a terapia para circunstâncias clínicas específicas. Como em qualquer outra situação clínica, devem-se consultar monografias dos produtos apropriados para verificar os regimes de dosagem ou os efeitos adversos, especialmente no caso de drogas ou equipamentos pouco familiares ou pouco usados. Embora haja evidência limitada a favor de determinadas terapias, há dados descrevendo o seu uso que podem permitir a sua consideração ao tratar pacientes sem transfusão de sangue, quando outras medidas não foram eficazes. O uso dos nomes comerciais nesse documento é feito apenas para identificação e informação e não significa qualquer endosso. Embora as opiniões aqui contidas tenham sido cuidadosamente revisadas e reflitam o conhecimento clínico e científico atual, elas estão sujeitas a mudanças.

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1. AVALIAÇÃO E CONDUTA INICIAL[1-7]

Alertas de ação clínica:

- Pacientes com sangramento ativo no trato gastrointestinal (GI) superior ou inferior representam quadros de emergência médica de alto risco que necessitam de uma intervenção imediata e intensiva.
- As prioridades do tratamento são manter a circulação e ao mesmo tempo identificar e suspender a fonte do sangramento.
- A determinação da gravidade do sangramento deve basear-se na magnitude estimada da hemorragia inicial e no grau do sangramento atual. Isso pode ser avaliado a partir do histórico e exame físico, condição hemodinâmica, sintomas atuais e achados endoscópicos.
- No paciente com sangramento, a avaliação inicial pode ser feita durante a ressuscitação.

A. Histórico do paciente[8-12]

1. Histórico médico e exame físico

a. Instabilidade hemodinâmica (p. ex., queda espontânea da pressão sanguínea, taquicardia persistente, taquipnéia, sensação de cabeça leve, hipoperfusão)
   (1) O histórico cardíaco pode ajudar a avaliar a reserva cardiorrespiratória
b. Histórico recente de quimioterapia ou radioterapia afetando o abdômen ou o reto (p. ex., processo maligno ginecológico, câncer de próstata)
c. Comorbidade com outras doenças (p. ex., hepática, renal) ou coagulopatia
d. Úlceras pépticas, varizes, gastrite, diverticulose ou pólipos no cólon, doenças inflamatórias no intestino, hemorróidas, doenças do fígado, uso de álcool, trauma/ferimento ou estresse recentes, vômito
e. Icterícia, ascite ou outros sinais de doença hepática, massa tumoral, ruído de uma lesão vascular abdominal, lesões purpúricas, petéquias, equimoses, telangiectasias, esplenomegalia

2. Características do sangramento

a. Fonte, início, e duração do sangramento, cor e aparência do sangue (p. ex., hematêmese, melena ou hematoquezia)
b. Volume da perda de sangue e grau observável da hemorragia (p. ex., condição durante a apresentação — tontura, desmaio, angina)

3. Histórico anterior de sangramento GI

a. Úlcera péptica infecciosa (infecção pelo *Helicobacter pylori*), varizes esofagogástricas, síndrome de Zollinger-Ellison (SZE), esofagite erosiva, malformações arteriovenosas (MAVs), telangiectasia hemorrágica hereditária (síndrome de Rendu-Osler-Weber), polipose intestinal (síndrome de Peutz-Jeghers), etc.
b. Cirurgia gastrointestinal anterior

4. Histórico de anemia

5. Histórico de doença GI/distúrbios de sangramento

a. Histórico pessoal e familiar
   (1) Doença hepática, câncer GI, etc.
   (2) Distúrbios de sangramento congênitos/adquiridos podem ser conhecidos desde o nascimento, sangramentos nasais, hematomas que surgem facilmente, tonsilectomia, extração de dentes, menorragia, cirurgia anterior, gravidez, etc.
   (3) Outras condições herdadas associadas com sangramento, como a síndrome de Rendu-Osler-Weber (telangiectasia hemorrágica hereditária) ou síndrome do nervo bolhoso esponjoso azul (doença de Bean)

6. Histórico das medicações usadas

a. Uso recente de anticoagulantes ou anti-agregantes plaquetários[13,14]
b. Uso recente de medicações associadas com sangramento de úlceras pépticas ou erosões (p. ex. AAS, medicamentos que contenham AAS, AINEs), especialmente em pacientes idosos[15-18]
c. Identifique outras medicações recentes ou interações medicamentosas que possam afetar adversamente a hemostasia (p. ex., esteróides, inibidores seletivos da recaptação de serotonina [ISRSs], antibióticos)[19,20]

B. Ressuscitação inicial

1. Proteja as vias aéreas

2. Oxigênio suplementar

a. Considere iniciar o oxigênio em alto fluxo para compensar a perda de glóbulos vermelhos

3. Controle de fluido/monitoração do volume (Veja também **3.B.**)

C. Avaliação laboratorial seletiva/triagem

1. Hemograma completo

2. TP (INR), TTP, tempo de sangramento com dispositivo de punção (segundo indicado)

3. Bioquímica sanguínea (incluindo nitrogênio uréico sanguíneo [BUN], creatinina)

4. Investigação adicional (segundo indicado)

a. Testes da função hepática
b. Testes da função renal
c. Testes de coagulação (se houver suspeita de distúrbios de sangramento)

D. Diagnóstico e localização do local de sangramento[21-23]

1. Quantidade de sangue perdido

a. Alguns indicadores de grande perda sanguínea:[24-26]
   (1) Hipotensão ortostática/taquicardia sugere uma perda de 10%-20% no volume [27]
   (2) Hipotensão, palidez, e taquicardia em repouso podem indicar uma perda de 30%-40% no volume
   (3) Acidose
   (4) Hematoquezia pode indicar a entrada de pelo menos 1000 ml de sangue no trato GI superior
   (5) Uréia sanguínea >25 mmol/L em pacientes sem doença renal prévia é um indicador de perda sanguínea significativa (talvez >1000 ml)[28]

2. Indicadores da fonte do sangramento

a. **Proporção do nitrogênio uréico sanguíneo/creatinina**[29,30]
   (1) Uma proporção elevada de BUN/creatinina (>36) indica hemorragia GI superior
b. **Hematêmese, hematoquezia e melena**
   (1) Hematêmese e/ou aspirado nasogástrico positivo sugerem hemorragia GI superior e constituem indicação para uma endoscopia de emergência
   (2) Melena pode ser indicativa de hemorragia GI tanto superior como inferior
   (3) Hematoquezia sugere sangramento GI inferior mas ocasionalmente resulta de sangramento GI superior intenso
   (4) Hematêmese com sangue vivo ou material semelhante à borra de café sugere sangramento GI superior
   (5) Hematêmese vermelha e acompanhada de hematoquezia (fezes marrons e/ou coágulos frescos pelo reto) sugerem sangramento ativo maciço do trato GI superior
c. **Indicações adicionais de lesões**
   (1) Histórico de gastrite, disfagia ou regurgitação pode sugerir refluxo gastroesofágico que pode levar à hemorragia por esofagite erosiva grave
   (2) Pacientes com antecedente de úlcera péptica que não passaram pela erradicação do *Helicobacter pylori;* pacientes com hipertensão portal que suspenderam os beta bloqueadores abruptamente
   (3) Pacientes usando AINEs (especialmente AAS) têm maior probabilidade de desenvolver ulceração gástrica ou duodenal bem como lesões no intestino grosso e delgado
   (4) Histórico de tosse, vômito ou náuseas antes do início do sangramento sugere laceração de Mallory-Weiss
   (5) Pacientes com antecedente de varizes esofágicas são mais propensos a apresentar novo sangramento das varizes ou um sangramento resultante de uma gastropatia hipertensiva portal
   (6) Dor pode sugerir uma lesão na mucosa como uma úlcera péptica
   (7) No caso de sangramento recorrente proveniente de um local desconhecido, apesar de avaliação diagnóstica prévia, deve-se considerar a possibilidade de tratar-se de malformações arteriovenosas ou lesões de Dieulafoy

E. Intervenções diagnósticas

Alertas de ação clínica:

- Tratamento sem transfusão de sangue alogênico envolve um total comprometimento em encontrar e estancar qualquer perda sanguínea. São necessárias investigação e terapia intensivas.
- Talvez não seja reconhecida a urgência clínica de um sangramento discreto mas persistente até que os mecanismos compensatórios falhem e haja queda da pressão arterial

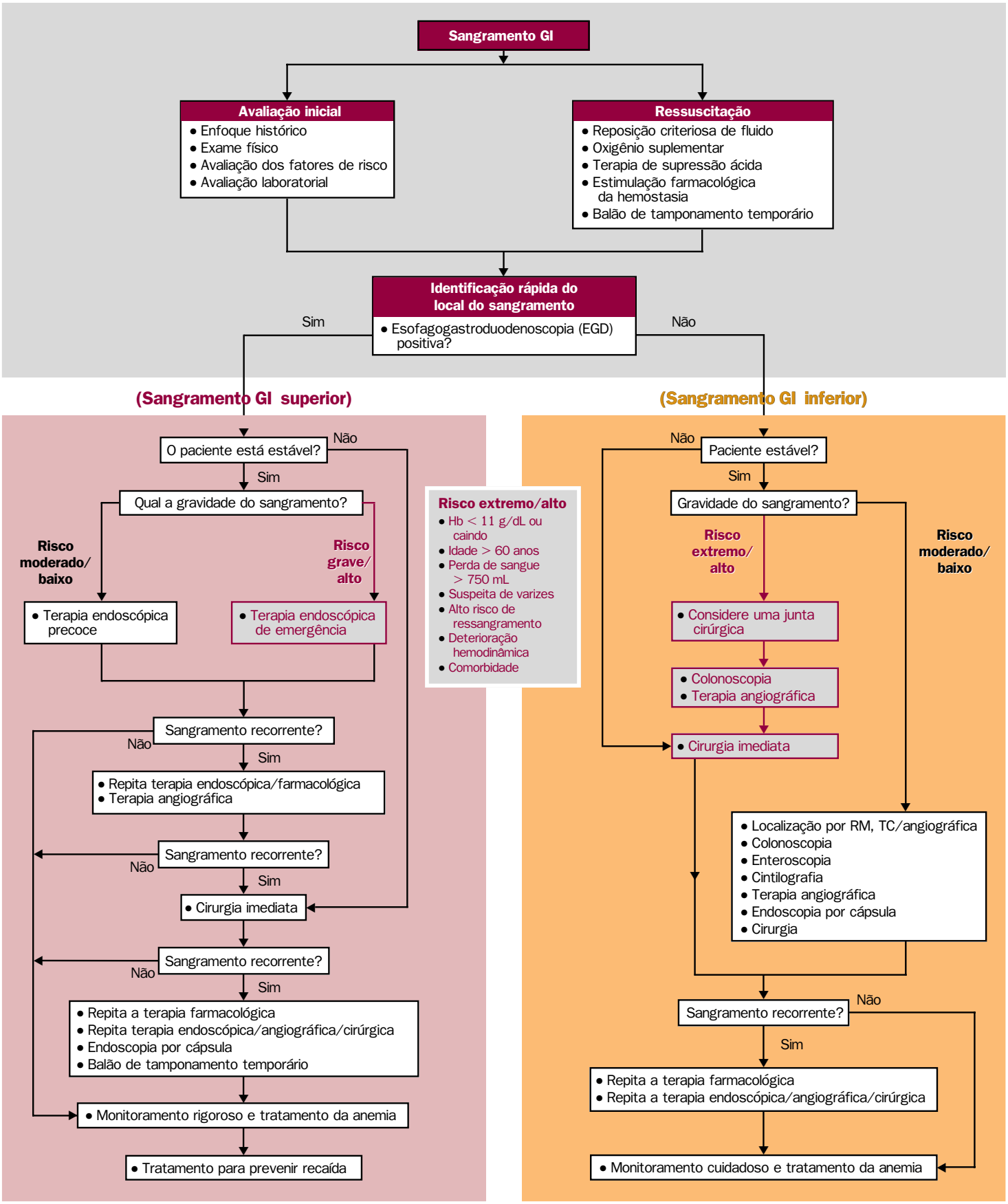
1. Lavagem/aspiração nasogástrica[31-33]

a. Se houver suspeita de sangramento GI superior indicada pelo aspirado nasogástrico (NG), realize a uma endoscopia de emergência; como rotina a aspiração NG é controversial

2. Exame anorretal[34]

a. Tônus retal, aparência das fezes e presença de qualquer massa

ALGORITMO PARA TRATAMENTO DE SANGRAMENTO GASTROINTESTINAL (GI) SEM SANGUE



Esse algoritmo descreve os cuidados básicos dos pacientes. A prática irá variar de acordo com a situação clínica, recursos locais, equipe e perícia.

3. **Endoscopia precoce**[35-42]
   a. Uma endoscopia precoce/urgente é definida como tal se for realizada nas primeiras 12 horas da admissão. Tem-se mostrado que a endoscopia precoce reduz a incidência de sangramento posterior e eleva as taxas de sobrevivência. Alguns pesquisadores recomendam que a endoscopia seja feita sem demora (dentro de 4 horas), especialmente em pacientes com sangramento, para reduzir a hospitalização e os custos[36,39,41,43,44] (Veja também **2.A.1.b.**)
   b. A aparência endoscópica de uma úlcera sangrante ou os sinais de uma hemorragia recente tem valor em determinar o prognóstico e orientar o tratamento.[43,45]
   c. Considere a administração imediata de eritromicina, antes da endoscopia, para melhorar a visualização.[46,47]
4. **Colonoscopia imediata**[48-54]
   a. Considere a realização de uma rápida limpeza intestinal. Complicações como perfuração são mais comuns em um cólon que não foi limpo, por causa da baixa visibilidade.
5. **Rápida angiografia/embolização**[55-60]
   Nota: Técnicas de estímulo de sangramento empregadas para melhorar o diagnóstico em pacientes estáveis com sangramentos obscuros recorrentes devem ser usadas com extrema cautela.[61-63] Se usadas, devem ser cercadas de precauções apropriadas, como por exemplo, realizadas em um local onde, se necessário, possa ser iniciada imediatamente uma ressuscitação, incluindo agentes de reversão, hidratação intravenosa e medidas terapêuticas para controlar o sangramento (angiográfica, endoscópica ou cirúrgica).
6. **Videoendoscopia por cápsula sem fio**[64-70]
   Nota: O uso da endoscopia por cápsula no início da avaliação do paciente permite um diagnóstico mais rápido e um tratamento melhor para o paciente. Isso também pode reduzir os custos associados com sangramentos obscuros.[71]
7. **RM (ressonância magnética) ou exames de tomografia computadorizada helicoidal (TC)**[72-75]
8. **Laparotomia e cirurgia exploratória precoces**[76]
   Nota: As intervenções diagnósticas mencionadas a seguir são em geral realizadas em circunstâncias eletivas.
9. **Enteróclise**[77,78]
10. **Enteroscopia**
    a. Enteroscopia com duplo balão[79,80]
    b. Push-enteroscopia[81-84]
    c. Enteroscopia intra-operatória [85]
11. **Imagem por cintilografia/radionuclídeo**[86-88]
    a. Eritrócitos marcados com tecnécio 99m[89,90]
    b. Colóide de enxofre marcado com tecnécio 99m[91]

F. Mantenha um alto nível de suspeita clínica de sangramento

1. **Controle seriado do nível de hemoglobina**
   a. Quedas no nível de hemoglobina requerem rápido esclarecimento da causa
   b. Quedas no hematócrito retardam o curso clínico e não são indicadores confiáveis da magnitude de um sangramento agudo mas podem ser úteis para a indicação de hemorragia em andamento
2. **Adote um limiar mais baixo para intervenção**
   a. Em pacientes que não podem ser transfundidos, para identificar e estancar o sangramento o mais cedo possível, considere uma intervenção endoscópica, radiológica ou cirúrgica baseando-se em sinais e sintomas menos específicos

2. CONTROLE IMEDIATO DO SANGRAMENTO

A. Diagnóstico e tratamento rápidos

1. **Endoscopia Imediata e terapia farmacológica**[92,93]
   a. Em pacientes com alto risco de novo sangramento ou morte, a endoscopia deve ser feita o mais cedo possível, assim que for seguro[94]
   b. A terapia endoscópica diligente agiliza a triagem e está associada à redução da perda de sangue, período de internação hospitalar, custos e risco de sangramento recorrente e cirurgia[38,41,44,48,95-98] (Veja também **1.E.3.a.**)
   c. Em casos de intenso sangramento devido à úlcera ou varizes, considere o tratamento empírico com alta dose de inibidor da bomba de prótons IV (IBP) ou octeotride/somatostatina como tratamento médico concomitante enquanto aguarda a endoscopia ou a cirurgia
2. **Tratamento cirúrgico imediato**
   a. Se o sangramento ativo não puder ser controlado pela terapia farmacológica, endoscópica ou angiográfica, ou se houver uma hemorragia exsanguínea, o paciente precisa de cirurgia urgente[99,100]
   b. Para minimizar a perda de sangue, considere limitar a cirurgia ao mínimo necessário para controlar a hemorragia
   c. É preferível considerar uma cirurgia definitiva imediata para estancar o sangramento do que adiá-la,[100-103] principalmente em pacientes com mais de 60 anos

3. CRITERIOSA RESSUSCITAÇÃO VOLÊMICA

Alertas de ação clínica:

- A imediata, mas criteriosa ressuscitação com fluidos em pacientes hemodinamicamente instáveis bem como oxigênio suplementar otimiza a circulação dos glóbulos vermelhos remanescentes e melhora o transporte de oxigênio.
- A causa mais comum de um paciente não responder bem à terapia com fluidos é uma hemorragia contínua.
- Mantenha a normovolemia e oxigenoterapia em pacientes anêmicos sem sangramento.

A. Expansores de volume isentos de sangue

1. **Cristalóides**
   a. Solução salina normal
   b. Lactato de Ringer
   Nota: Em quantidades moderadas, os cristalóides não estão associados com efeitos colaterais significantes, particularmente sobre a hemostasia. Há evidência laboratorial de que infusões de cristalóides podem induzir um estado de hipercoagulabilidade.[104,105] É mais provável que grandes volumes de cristalóides causem formação de edema, prejudiquem a função pulmonar e leve à coagulapatia dilucional.
2. **Colóides**
   a. Pentastarch/hetastarch (hidroxietilamido)
   b. Gelatina
   c. Dextran
   Notas:
   1. Hidroxietilas de amido (HES) de alto peso molecular (p. ex., 450 kDa) com elevado grau de substituição (DS: 0.7), outras preparações de HES fortemente substituídas e dextrans podem elevar o risco de sangramento em pacientes que têm anormalidades de coagulação congênitas ou adquiridas de forma dose dependente.[106,107]
   2. Enquanto todos os colóides e cristalóides diluem plaquetas e fatores de coagulação, dextrans estão associados à tendência ao sangramento por inibirem a agregação de plaqueta, reduzindo a atividade do fator VIII e promovendo fibrinólise.[108]
3. **Oxigenoterapia**[109,110] (quando disponível para uso clínico)
   Notas:
   1. Evite sobrecarga circulatória, especialmente em pacientes profundamente anêmicos[111,112] .Deve ser evitada a administração de fluidos apegando-se apenas a um protocolo sem avaliação clínica contínua.
   2. Mesmo durante hipotensão relativa, a circulação de sangue no sistema microvascular e a oxigenação nem sempre dependem da pressão sanguínea.[113,114]

B. Evite excessiva reposição de fluidos

1. **A normalização da pressão sanguínea pode agravar o sangramento**
   a. Na hemorragia descontrolada, há evidência de que a elevação da pressão sanguínea (p. ex., por ressuscitação com fluido, medicamentos vasopressores) antes do controle definitivo do sangramento pode resultar em ressangramento progressivo e repetido[115-118]
   b. A evidência atual sugere que a rápida administração de fluidos na circulação diante de sangramento em curso pode temporariamente restaurar os sinais vitais, mas causa perda de vasoconstrição auto-reguladora e maior perda de sangue no local (ou nos locais) de sangramento, bem como perda mais rápida dos fatores de coagulação. O aumento da pressão sanguínea e do fluxo no local (nos locais) de sangramento arrastará os coágulos e os tampões de plaquetas[119,120]
   c. A evidência a partir de estudos de gastroenterologia e de traumatologia sugere no caso de hemorragia aguda de alto risco, considerar a possibilidade de realizar uma ressuscitação controlada moderada e a tolerância à hipotensão leve a moderada, ou seja, pressão sanguínea no nível mais baixo possível que mantenha a perfusão dos tecidos (p. ex., pressão sistólica de 90-100 mm Hg em um paciente normotenso)[115,120-123] até que o sangramento possa ser definitivamente controlado

4. ESTIMULAÇÃO FARMACOLÓGICA DA HEMOSTASIA

A. Aumente a atividade dos fatores de coagulação

1. **Desmopressina**[6,124-127] (p.ex., DDAVP®, Octostim®, Stimate®)
2. **Vitamina K**[128-130]

   Nota: Pacientes podem ter deficiência de vitamina K devido a uma dieta alimentar inadequada/má nutrição, absorção limitada (p.ex., pacientes debilitados),[131] obstrução biliar, uso de antibióticos, anticoagulantes (p.ex., nicoumalone, varfarina).
3. **Fator VII recombinante ativado (rFVIIa)** (p.ex., NovoSeven®, NiaStase®)
   a. O uso precoce do rFVIIa pode salvar a vida de pacientes não hemofílicos sem distúrbios hereditários de sangramento que estão sangrando em locais com possibilidades limitadas de ser realizada uma hemostasia endoscópica[132]
   b. O rFVIIa tem sido usado como terapia coadjuvante para reduzir a perda de sangue em pacientes não hemofílicos em várias situações clínicas incluindo sangramento de úlcera,[133] varicoso,[134-136] diverticular;[137] cirurgia;[138-142] sangramento pós-operatório;[143-146] coagulopatia associada com doenças hepáticas;[147-151] falência renal;[145,152,153] trombocitopenia;[154-158] distúrbios congênitos ou adquiridos da função plaquetária;[159-161] e tendências adquiridas ao sangramento [162-164]
   c. Considere o uso do rFVIIa em casos de coagulação intravascular disseminada[165,166]
   d. Embora certas características do rFVIIa possam, teoricamente, aumentar o risco de trombose, a análise dos dados clínicos existentes sugere um perfil altamente favorável de segurança e eficácia.[167] Eventos trombóticos foram relatados em pacientes com predisposição para complicações tromboembólicas.[168] No caso de pacientes de risco, considere o uso de doses mais baixas do medicamento
4. **Tratamento dos distúrbios hemorrágicos congênitos ou adquiridos**
   a. Terapia de reposição de fator de coagulação

   Nota: Os fatores VIIa, VIII, IX estão disponíveis na forma de produtos recombinantes.
   b. Crioprecipitado

B. Reverta a anticoagulação

1. **Tratamento clínico**
   a. Vitamina K (fitonadiona)[169]
   b. Concentrado do complexo protrombínico[170-172] (p. ex., Autoplex®, Beriplex®)
   c. Fator VIIa recombinante de coagulação [173-175] ou IX[176,177] (p. ex., BeneFix®, Proplex T®)

C. Terapia de supressão ácida (Eleve o pH gástrico)

1. **Inibidores da bomba de prótons (PPIs), antagonistas dos receptores H_2 (ARH_2), etc.** (Veja **5.** e **6.**)

D. Induza a vasoconstrição esplâncnica

1. **Somatostatina, octeotride, vasopressina, etc.** (veja **5.** e **6.**)

E. Outros agentes com efeito hemostático

1. **Estrogênios conjugados**[178-183] (p. ex, Premarin®)

   Nota: Os estrogênios conjugados ativam o processo de coagulação, encurtam o tempo de sangramentos prolongados, e suspendem o sangramento em pacientes com disfunção plaquetária decorrente de uremia.
2. **Eritropoetina recombinante** (p. ex., Procrit®, Eprex®)

   Notas:
   1. Relata-se que a eritropoetina promove a hemóstase no caso de sangramento proveniente de lesões difusas do trato GI (p. ex., angiodisplasias, proctite por radiação, adenocarcinoma).[184]
   2. Eritropoetina recombinante pode produzir um aumento na contagem e reatividade das plaquetas que é moderado, transitório e dose-dependente, dentro dos limites normais, durante o tratamento. Isso regride durante o curso da terapia continuada.[185,186]
3. **Considere a terapia estimulante da trombopoese**
   a. Interleucina-11 humana recombinante[187] (p. ex., Neumega®)

F. Altere/descontinue o uso de AINEs[188-190]

1. **Descontinuação/substituição/redução da dose**
   a. Descontinuação/redução da dose de aspirina, medicamentos que contenham aspirina, AINEs, anticoagulantes, outros medicamentos e fórmulas fitoterápicas associados com sangramento (p. ex., alho, ginkgo biloba, ginseng)
   b. Para pacientes que necessitem de analgésico e que estejam com risco moderado de recidiva do sangramento, considere a substituição por um analgésico sem AINE, AINEs menos gastrotóxicos (p. ex., etodolac, salicilato não acetilado), associação de agentes gastroprotetores (p. ex., IBP, misoprostol, doses-duplas de ARH_2), ou inibidores específicos da COX-2 (coxibs)

G. Iniba a fibrinólise

1. **Ácido tranexâmico**[191-198] (p. ex., Transamin®, Cyklokapron®)

   Notas:
   1. Há evidência de que em casos de hemorragia GI alta aguda, a elevada atividade fibrinolítica está relacionada com o aumento do sangramento.[199]
   2. Embora haja relatos que consideram a possibilidade de aumento do risco de trombose com o uso de antifibrinolíticos, nenhum estudo controlado indica aumento desse risco.
   3. Tendo em vista que o sangramento apresenta riscos mais graves e imediatos do que a morbidade associada com as complicações da trombose, deve-se considerar o uso a curto prazo do ácido tranexâmico, talvez em combinação com um antagonista dos receptores H_2(ARH_2).
2. **Ácido epsilon-aminocapróico**[200-203] (p.ex., Amicar®)

5. SANGRAMENTO DO TRATO GI SUPERIOR

Alertas de ação clínica:

- Os princípios gerais fundamentais e terapêuticos delineados no início desse documento devem ser aplicados nos cuidados clínicos da hemorragia do trato GI superior.
- Se um especialista em endoscopia não estiver disponível, considere uma cirurgia ou administre agentes farmacológicos (p. ex., terapia de supressão ácida em alta dosagem, octeotride, terlipressina), use balão de tamponamento e transfira o paciente.
- A falha em parar rapidamente uma hemorragia grave de úlcera emergente e/ou refratária com terapia endoscópica (p. ex., térmica, injeção, mecânica ou terapia combinada), farmacológica, ou angiográfica deve levar imediatamente a uma intervenção cirúrgica. De modo geral, para pacientes com sangramento evite a postura de "observar e esperar".
- Se for necessário um procedimento cirúrgico, consulte também o documento "Estratégias clínicas para evitar e controlar hemorragias e anemia sem transfusão de sangue em pacientes cirúrgicos".[204]

A. Hemorragia de úlcera péptica[94,205,206]

1. **Terapia farmacológica de supressão ácida** (em combinação com endoscopia)
   a. **Inibidores da bomba de prótons (PPIs)**[207-211] (p. ex., omeprazol [Losec®], pantoprazol [Panto®])
   b. **Antagonistas do receptor H_2 da histamina (ARH_2)**[212,213] (p. ex., cimetidina [p. ex., Tagamet®], ranitidina [p. ex., Zantac®])
   c. **Antiácidos**

   Notas:
   1. Os agentes farmacológicos podem ser administrados em combinação com a terapia endoscópica. Há indícios sugerindo que o uso de PPIs antes e depois da terapia endoscópica melhora o resultado, especialmente se houver possibilidade de demora antes da endoscopia.[214-216]
   2. PPIs são mais eficazes que ARH_2 e antiácidos.
2. **Terapia endoscópica**[217-219]
   a. **Métodos térmicos/de eletrocoagulação**
      (1) Heater probe (sonda térmica)[214,220-222]
      (2) Eletrocoagulação monopolar/multipolar[223-227]
         i. *Injeção de gold probe™ (injeção e cateter eletro-hemostático)*[228,229]
      (3) Coagulação com plasma de argônio[230-232]
      (4) Coagulação usando microondas[233]
      (5) Terapia a *laser*[218,234,235]

      Nota: Veja "Terapia combinada" abaixo.
   b. **Escleroterapia por injeção**
      (1) Epinefrina[236-238]
      (2) Epinefrina e trombina[239,240]
      (3) Epinefrina e polidocanol[241-243]
      (4) Cola de fibrina[244,245] (p. ex., Beriplast®, Tisseel®)

c. **Hemóstase/oclusão mecânica**

(1) Ligadura elástica[246-248]

(2) Clipes hemostáticos endoscópicos (endoclipes/hemoclipes)[242,249-252]

(3) Considere o balão de tamponamento como medida temporária para controlar o sangramento enquanto espera uma intervenção hemostática definitiva[253,254]

d. **Terapia combinada**

(1) Injeção de epinefrina e termocoagulação[215,228,229,238,255-259]

(2) Terapia de injeção e hemóstase mecânica[260,261]

Notas:

1. Pacientes com úlceras sangrando ativamente, úlceras com vasos visíveis sem sangramento e úlceras com coágulos aderentes sem sangramento devem receber uma terapia combinada (p. ex., injeção de epinefrina seguida de abordagens hemostáticas mecânicas ou térmicas).[256,258,259]
2. Injeção inicial de epinefrina na base de úlceras sangrando ativamente diminui o sangramento e permite uma melhor visualização do local de sangramento para a coagulação térmica. Para úlceras com coágulos aderentes sem sangramento, a injeção de epinefrina ajuda a prevenir o sangramento durante a dissecção com guilhotina e desbaste do coágulo sobrejacente.[255]

3. **Tratamento cirúrgico**[204,262,263]

a. **Cirurgia de emergência**

(1) Colocação de patch sobre vasos sangrantes[99,101,264-266]

(2) Vagotomia altamente seletiva

(3) Ressecção gástrica[267]

Notas:

1. A cirurgia deve ser feita se o sangramento não puder ser controlado por endoscopia ou se ocorrer um ressangramento após a hemóstase endoscópica.
2. O procedimento cirúrgico escolhido depende de que operação pode ser feita rapidamente para controlar a hemorragia. Considere a realização de procedimentos extensivos em estágios.[6] Para pequenas úlceras, é adequada a colocação de patch ou extirpação da úlcera. Para úlceras grandes, pode ser necessária a gastrectomia para garantir a hemóstase. A cirurgia deve ser limitada ao mínimo necessário com o objetivo de parar o sangramento.

4. **Terapia angiográfica/radiológica**

a. **Embolização angiográfica**[268]

5. **Minimizar o risco de hemorragia recorrente**

a. Uso seletivo de um segundo exame/terapia endoscópica[269,270]

b. Administração de PPI ou ARH_2 após a terapia endoscópica[209,271-274]

c. *Combinação* seletiva de tratamento endoscópico[255,275]

d. Exame para detectar infecção pelo *Helicobacter pylori* e erradicação[276-278]

Nota: Previna o sangramento recorrente em usuários de alto risco de AINEs.[279-281]

B. Sangramento de varizes gastroesofágicas[282,283]

1. **Terapia farmacológica precoce [284] combinada com terapia endoscópica**[285-287]

a. Somatostatina/octeotride[288-291]

Nota: Há evidências de que a terapia com octeotride iniciada assim que o paciente com suspeita de sangramento varicoso dá entrada no hospital, em combinação com métodos endoscópicos, ajudará no pronto controle da hemorragia e evitará o sangramento recorrente imediato.[292-294]

b. Terlipressina[295-297] usada só ou com nitroglicerina[298-300]

c. Vasopressina[301,302] usada só ou com nitroglicerina[303,304]

2. **Tratamento de varizes esofágicas**

a. Ligadura elástica[305-308]

b. Escleroterapia por injeção[309-312]

Nota: Ligadura endoscópica de varize tem-se mostrado superior à escleroterapia nos casos mais graves, inclusive sangramento recorrente.

c. Terapia combinada

(1) Ligadura elástica (ou escleroterapia) e somatostatina/octeotride[92,291,293]

(2) Ligadura elástica (ou escleroterapia) e coagulação com plasma de argônio[313,314]

(3) Escleroterapia e injeção de cianoacrilato[315,316]

d. Balão de tamponamento[317-321]

Nota: Embora a colocação de balões hemostáticos possa promover o controle imediato do sangramento em quase todos os tipos de varizes, eles devem ser encarados como uma medida estabilizadora temporária; há alto risco de ressangramento. O controle definitivo da hemorragia não deve ser adiado.

3. **Tratamento de varizes gástricas**[305,309,322]

a. Terapia endoscópica de injeção[309,323]

(1) Cianoacrilato[324-327] (p. ex., Dermabond®, Glubran®, Histoacryl®)

(2) Cola de fibrina/trombina[328,329] (p. ex., Beriplast®, Tisseel®)

b. Ligadura elástica[330,331]

c. Combinação ligadura com alça (*detachable snare*) e terapia de injeção[332]

d. Balão de tamponamento[317,321,333,334]

4. **Tratamento cirúrgico**

a. Shunting esplenorrenal/portacaval/portossistêmico[335-339]

b. Transeção/desvascularização[340]

5. **Tratamento radiológico**

a. Shunt portossistêmico intra-hepático transjugular (TIPS)[341-344]

b. Obliteração transvenosa retrógrada com balão encravado[345-348]

c. Escleroterapia transcatéter[349,350]

6. **Prevenção de sangramento varicoso recorrente**

a. Ligadura elástica[351-353]

b. Escleroterapia[354-356]

c. Terapia com betabloqueadores[357]

(1) Propranolol[358,359]

(2) Nadolol[360,361]

Nota: O uso de uma combinação de técnicas endoscópicas e farmacológicas pode ser mais eficaz que a monoterapia para a profilaxia de ressangramento varicoso.[360-363]

d. Terapia antibiótica profilática[364,365]

e. Shunt portossistêmico intra-hepático transjugular profilático (TIPS)[366,367] isolado ou com angioterapia associada[368]

f. Cirurgia de transplante de fígado[204]

Nota: Prevenção de ***um primeiro sangramento das varizes*** (profilaxia primária) pode ser conseguida usando-se betabloqueadores não cardioseletivos (p. ex., propranolol, nadolol), ligadura elástica endoscópica, associação de ligadura e betabloador (para varizes grandes), associação de betabloqueador e mononitrato de isosorbida, ou escleroterapia.

C. Lacerações de Mallory-Weiss

1. **Ligadura elástica**[369-372]
2. **Terapia de injeção de epinefrina**[373-375]
3. **Hemoclipe**[373,376]
4. **Eletrocoagulação multipolar**[377]
5. **Balão de tamponamento**[378]

D. Lesão de Dieulafoy

1. **Ligadura elástica**[379-382]
2. **Hemoclipe**[382-385]
3. **Combinação de injeção de epinefrina e terapia com sonda térmica**[384,386]
4. **Considere balão de tamponamento temporário**[387]

E. Angiomas gastrointestinais e outras condições

1. **Ectasia vascular antral gástrica (estômago em melancia)**[388]

a. Coagulação com plasma de argônio[389-391]

b. Terapia com *laser*[392]

c. Terapia farmacológica[179,193]

2. **Telangiectasia hemorrágica hereditária /angiodisplasia/malformações vasculares**

a. Terapia farmacológica[181-183,193,201,203]

b. Termocoagulação[393,394]

c. Considere a angiografia e embolização[395]

3. **Gastrite hemorrágica aguda**

a. Descontinue AINEs

b. Bloqueadores H_2, PPIs, sucralfato, antiácidos

c. Terapia com antibiótico, em presença de *Helicobacter pylori*

d. Somatostatina/octeotride

e. Vasopressina

f. Considere a gastrectomia subtotal ou total

4. **Câncer no esôfago (incluindo o esôfago de Barrett)**

a. Coagulação com plasma de argônio[396-398]

b. Eletrocoagulação térmica/multipolar[399]

c. Terapia fotodinâmica/*laser*[400,401]

d. Ressecção cirúrgica

5. **Fístula aorto-entérica**

a. Oclusão temporária[402,403]

b. Tratamento angiográfico ou cirúrgico/endovascular[404,405]

6. **Hemobilia**

a. Arteriografia e embolização[406]

7. **Síndrome do nervo bolhoso esponjoso azul (doença de Bean)**

a. Tratamento endoscópico[407-409]

b. Tratamento cirúrgico[410,411]

6. SANGRAMENTO DO TRATO GI INFERIOR[412]

Alertas de ação clínica:

- Os princípios gerais fundamentais e terapêuticos delineados no início deste documento devem ser aplicados nos cuidados clínicos do sangramento do trato GI inferior.
- Os dados apóiam uma abordagem precoce e agressiva para a determinação do local de sangramento antes que a perda de sangue se torne significativa.
- A intervenção cirúrgica deve ser feita sem demora em pacientes com sangramento que não respondam à terapia endoscópica e/ou angiográfica. Em casos de sangramento grave, uma colectomia total ou subtotal imediata pode salvar a vida.
- Se for necessário um procedimento cirúrgico, consulte também o documento "Estratégias clínicas para evitar e controlar hemorragias e anemia sem transfusão de sangue em pacientes cirúrgicos".[204]

A. Terapia clínica

1. **Descontinuação/substituição de aspirina, AINEs, anticoagulantes e outras medicações**
2. **Terapia com somatostatina/octeotride**[413-415]

B. Hemorragia diverticular

1. **Terapia endoscópica**[416,417]
   a. Terapia térmica/coagulação por colonoscopia
      (1) Sonda térmica de contato[54,418]
      (2) Eletrocoagulação bipolar[54,419,420]
      (3) Terapia com *laser*[418,421]
   b. Terapia de injeção[418,422,423]
   c. Hemóstase mecânica/oclusão
      (1) Ligadura elástica[424]
      (2) Hemoclipe[425,426]
   d. Terapia combinada
      (1) Terapia de coagulação ou hemóstase mecânica e escleroterapia por injeção[54,427]
2. **Terapia angiográfica**
   a. Embolização angiográfica[428,429]
   b. Infusão de agentes vasoconstritores
      (1) Terlipressina/vasopressina[430,431]

   Notas:
   1. Infusão de terlipressina/vasopressina pode ser usada para conseguir um controle temporário do sangramento e permitir intervenção cirúrgica. A embolização angiográfica evita os efeitos vasoconstritores da vasopressina em pacientes com isquemia miocárdica, hipertensão, etc.
   2. Quando a fonte de sangramento é obscura, o sangramento induzido deve ser empregado com extrema cautela em pacientes anêmicos que não podem ser transfundidos.
3. **Cirurgia**[432,433]

C. Angiodisplasias (ectasia vascular, malformações arteriovenosas)

1. **Terapia endoscópica**
   a. Termocoagulação por colonoscopia /eletrocoagulação[434,435]
   b. Terapia de injeção[436]
   c. Ligadura elástica[437]
2. **Terapia farmacológica**
   a. Somatostatina/octeotride[414,415]
   b. Estrogênios conjugados[178]
   c. Fator recombinante ativado VII (rFVIIa)[164]
   d. Considere o ácido tranexâmico[193,194]
   e. Considere a terapia com talidomida[438]
3. **Terapia angiográfica**[439,440]
4. **Cirurgia**

D. Hemorragia anorretal

1. **Hemorróidas externas/internas**
   a. Ligadura elástica[441,442] isolada ou associada com escleroterapia[443]
   b. Hemorroidectomia/hemorroidopexia com grampo[444,445]
   c. Extirpação cirúrgica[446]
   d. Termocoagulação/eletrocoagulação[447-451]
   e. Bisturi ultra-sônico[452,453]
   f. Outras técnicas hemostáticas[454]
2. **Proctite/colite induzida por radiação**
   a. Terapia com formalina[455-457] (i.e., solução aquosa de formaldeído a 4%)
   b. Coagulação com plasma de argônio[458-460]
   c. Eletrocoagulação[461]
   d. Terapia com *laser*[462]
   e. Tratamento cirúrgico[463,464]
   f. Crioterapia[465]
3. **Varizes anorretais**
   a. Coagulação com plasma de argônio[466]
   b. Ligadura elástica[467,468]
   c. Injeção de cianoacrilato[469] (e.g., Dermabond®, Glubran®, Histoacryl®)
   d. Shunt portosistêmico intra-hepático transjugular (TIPS)[470]
   e. Cirurgia

E. Sangramento localizado pós-polipectomia

1. **Terapia endoscópica**
   a. Termo ou eletrocoagulação colonoscópica isolada ou combinada com injeção de epinefrina[471-473]
   b. Ligadura elástica[474,475]
   c. Hemoclipe/ ligadura com alça (*detachable snare*)[476,477]
   d. Cola de fibrina[478] (e.g., Beriplast®, Tisseel®)
2. **Terapia farmacológica**
   a. Reduzir/suspender terapia de anticoagulação[479]
   b. Considere o fator recombinante ativado VII (rFVIIa)[149]
3. **Terapia angiográfica**[440,471]
4. **Cirurgia**

F. Doenças inflamatórias intestinais (inclusive RCUI e Crohn)

1. **Diagnóstico/localização do sangramento**
   a. Colonoscopia[480]
   b. TC/angiografia[481]
   c. Endoscopia por cápsula sem fio[482-484] (para fontes no intestino delgado)
2. **Terapia hemostática**
   a. Escleroterapia por injeção[485]
   b. Fator recombinante ativado VII (rFVIIa)[146,486]
   c. Considere embolização angiográfica[487]
   d. Considere terapia com infliximab[488,489] (e.g., Remicade®)
   e. Ressecção cirúrgica[490-492]

G. Lesão de Dieulafoy

1. **Endoloop endoscópico**[493]

H. Divertículo de Meckel

1. **Cintilografia para pesquisa de divertículo de Meckel ou endoscopia por cápsula sem fio**[494,495]
2. **Extirpação cirúrgica minimamente invasiva**[496,497]

7. EVITE ANEMIA IATROGÊNICA

A. Flebotomia diagnóstica restritiva[498]

1. **Realize apenas os exames essenciais**[499]
2. **Exames de sangue coordenados e consolidados**[500]
   a. Minimize a freqüência de amostras de diagnóstico[501]
   b. Testes múltiplos por amostra[502]
3. **Minimize o volume de amostras de sangue para diagnóstico**
   a. Tubos de flebotomia pediátrica (pequeno volume) para os adultos[503]
   b. Microcoletagem de sangue/técnicas de microquímica[504,505]

8. TRATAMENTO DA ANEMIA

Alertas de ação clínica:

- É melhor ser cauteloso e aproveitar a primeira oportunidade que surgir para investigar e controlar a perda sanguínea de forma agressiva e sistemática do que tentar tratar a anemia grave depois que já ocorreu uma perda maciça de sangue.
- Se for necessário o tratamento em uma UTI, consulte também o documento "Estratégias Clínicas para Controlar Hemorragias e Anemia sem Transfusão de Sangue em Pacientes Criticamente Doentes".[506]
- Em casos agudos, as técnicas de tratamento de anemia que serão descritas a seguir foram usadas com sucesso, em combinação com outras modalidades (p. ex., otimização do transporte de oxigênio, minimização do consumo de oxigênio).

A. Terapia precoce com estimulantes eritropoéticos

1. **Eritropoetina ou darbepoetina alfa**
   a. Para acelerar a recuperação em casos de anemia aguda, relata-se o uso de doses de eritropoetina recombinante (rHuEPO) que variam de 150 a mais de 600 U/kg/dia[36,109,507-511]
   b. Um estudo controlado e randomizado, envolvendo 160 pacientes clínicos e cirúrgicos em UTI, demonstrou que o seguinte esquema de rHuEPO reduziu de forma significativa a taxa de transfusão de sangue: doses diárias de 300 U/kg/dia, durante 5 dias, seguidas pelo uso da mesma dose em dias alternados, durante um período mínimo de 2 semanas[512]
   c. Um estudo controlado e randomizado envolvendo 30 pacientes com anemia causada por hemorragia GI mostrou que a associação da rHuEPO com ferro IM acelerou de forma significativa a correção da anemia quando comparado com o uso isolado de ferro[513]
   d. Alguns pacientes necessitam de doses mais altas de rHuEPO para apresentar uma resposta adequada. Nos pacientes em estado grave, há evidência sugestiva de que doses de rHuEPO a intervalos freqüentes (p. ex., 150-300 U/kg/dia) podem ser mais eficientes que uma única dose semanal (p. ex., 600 U/kg).[507] Se não puder identificar ou corrigir a causa da baixa resposta à rHuEPO, considere o uso de uma dose mais alta[508,514-518]
   e. Para anemia grave, o uso concomitante de ferro IV potencializa a resposta aos agentes estimulantes da eritropoese.[519-521] O tratamento agressivo da anemia não deve ser retardado até que o nível de hemoglobina tenha chegado a níveis críticos.[522]
   f. Para os casos de anemia aguda severa considere a administração de eritropoetina inicialmente por via IV e em seguida por doses subcutâneas. Por meio da via IV atingem-se concentrações mais altas de eritropoetina no plasma, ao passo que a via subcutânea provê níveis mais estáveis[509,523-525]
   g. Em pacientes com doença inflamatória intestinal (DII), a dose terapêutica equivalente a 400-900 U/kg/semana de rHuEPO foi considerada como sendo 2.0-4.5 µg/kg/semana de darbepoetina alfa (DPO)[526]

Notas:

1. A terapia precoce com estimulantes eritropoéticos compensará a demora de uma resposta adequada pela medula óssea.
2. Além da deficiência de ferro, outros fatores que contribuem para uma resposta insatisfatória ao tratamento com estimulantes eritropoéticos incluem infecção, processo inflamatório ou maligno, perda de sangue e doença hematológica.[527,528]
3. Em pacientes com doença renal crônica ou hipertensão, os agentes estimulantes da eritropoese estão associados com o aumento da hipertensão. Monitore a hipertensão e considere iniciar ou aumentar a terapia anti-hipertensiva.
4. Têm surgido indicações de que a administração sistêmica de eritropoetina recombinante pode produzir efeitos de proteção cardíaca e renal[529,530] independentemente do nível de hemoglobina.
5. A aplasia pura de série vermelha é uma complicação rara restrita principalmente a pacientes com insuficiência renal crônica que recebem terapia subcutânea prolongada com eritropoetina (i.e., pacientes de hemodiálise renal).[531]

B. Terapia à base de ferro e suplemento hematínico[532]

1. **Ferro intravenoso (IV)**[526,533-535] (use a dose-teste)

Notas:

1. A administração intravenosa melhora a biodisponibilidade, aumenta rapidamente as reservas, evita uma potencial absorção deficiente ou irritação gástrica (p. ex., ferro oral).
2. Depois da dose-teste, administre ferro dextrano diluído em solução salina normal (p. ex., 500 ml) e retarde a infusão IV (p. ex., durante 1-8 horas) para reduzir o risco de reação adversa.[536-538]

2. **Ácido fólico**
3. **Vitamina B_{12}**

9. TOLERÂNCIA À ANEMIA

A. Anemia normovolêmica moderada é bem tolerada

1. **A anemia euvolêmica moderada é bem tolerada em pacientes hemodinamicamente estáveis portadores de doenças coexistentes**[539-543]
2. **O limiar para transfusão de 10/30 não tem base científica**[544-546]

B. Mecanismos compensatórios na anemia normovolêmica[547]

1. **Débito cardíaco aumentado**
2. **Redistribuição do fluxo sanguíneo**
3. **Aumento da extração de oxigênio pelos tecidos**
4. **Diminuição da afinidade da hemoglobina pelo oxigênio**

C. Efeitos da transfusão de glóbulos vermelhos armazenados

1. **Reversão da resposta hipercoagulável à hemorragia**
   a. Há evidência de que a hemorragia do trato GI superior induz uma resposta fisiológica local que pode atuar de maneira protetora para promover a hemostasia: inibição da secreção de ácido[548] e um estado hipercoagulável.[549] A transfusão de sangue armazenado (anticoagulado com citrato) reverte o estado hipercoagulável do sangue, resultando em recidiva do sangramento[115,117,550]
2. **Capacidade de liberação de oxigênio prejudicada**
   a. Glóbulos vermelhos armazenados têm reduzida capacidade de liberação de oxigênio (afinidade por oxigênio aumentada) por causa dos níveis reduzidos de 2,3-DPG. Isso talvez seja reversível em 24-48 horas[551-553]
3. **Outros efeitos clínicos adversos**
   a. A transfusão de sangue alogênico está associada a um aumento no risco de infecção,[554-557] a um aumento no período de internação,[558] à reincidência de câncer[559-562] e ao retardamento da cicatrização de feridas[563]. Além disso, está independentemente associada com uma mortalidade mais alta[115,564-569]

Referências

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Controle imediato do sangramento

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Criteriosa ressuscitação volêmica

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