The management of rectal bleeding following transrectal prostate biopsy: A review of the current literature

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Abstract

Introduction: Since the advent of prostate-specific antigen (PSA)-based testing, transrectal ultrasound (TRUS)-guided prostate biopsy has become a standard part of the diagnostic pathway for prostate cancer (PCa). Rectal bleeding is one of the common side effects of this transrectal route. While rectal bleeding is usually mild and self-limiting, it can be life-threatening. In this article, we examine rectal bleeding post TRUS-guided prostate biopsy and explore the literature to evaluate techniques and strategies aimed at preventing and managing this common and important complication.
Methods: A PubMed literature search was carried out using the keywords "transrectal-prostate-biopsy-bleed." A search of the bibliography of reviewed studies was also conducted. Additionally, papers in non-PubMed-listed journals of which the authors were aware were appraised.
Results: Numerous modifiable risk factors for this bleeding complication exist, particularly anticoagulants/antiplatelets and the number of core biopsies taken. Successfully described corrective measures for such rectal bleeding include tamponade (digital/packs/catheter/tampon/condom), endoscopic sclerotherapy/banding/clipping, radiological embolization, and surgical intervention.
Conclusions: We advocate early consultation with the colorectal/gastroenterology and interventional radiology services and a progressive, stepwise approach to the management of post-biopsy rectal bleeding, starting with resuscitation and conservative tamponade measures, moving to endoscopic hemostasis ± radiological embolization ± transanal surgical methods. Given the infrequent but serious nature of major rectal bleeding after TRUS biopsy, we recommend the establishment of centralized databases or registries forthwith to prospectively capture such data. To the best of our knowledge, this is the first comprehensive look specifically at the management of post-TRUS biopsy rectal bleeding.

Introduction

Central to PSA-based testing for PCa is the role of TRUS-guided prostate biopsy. It is estimated that more than one million TRUS-guided prostate biopsies are currently performed annually in both the USA and Europe.[1] Furthermore, active surveillance (AS) protocols for low-risk PCa have become established in various guidelines, including the European Association of Urology (EAU) PCa guidelines.[2] AS typically involves repeat prostate biopsies at predefined follow-up intervals, often as frequently as yearly.[3,4] Thus, as AS gains increasing acceptance, the number of prostate biopsies will increase.[5]

TRUS-guided prostate biopsy can cause several potential complications, including haematospermia (37.4%), haematuria (14.5%), rectal bleeding < 2 days (2.2%), rectal bleeding > 2 days +/- intervention (0.7%), sepsis (0.8%) or urinary retention (0.2%).[2] The literature reports higher rectal bleeding rates – in one prospective study, 25% of patients experienced a rectal bleed after biopsy.[6] Enlund et al. also showed a 22% immediate post biopsy rate of haematochezia which fell to 3% at three days and 0.5% at seven days.[7] Massive rectal haemorrhage post-biopsy has been reported in up to 1% of cases.[8] Al-Otaibi et al. report a case of rectal bleeding precipitating disseminated intravascular coagulation which required intensive care unit (ICU) treatment and correction of acute renal failure, pulmonary oedema and atrial fibrillation.[9] A large anterior rectal wall haematoma with near total occlusion of the rectal lumen following a TRUS-guided prostate biopsy has also been reported and sizeable prevesical space of Retzius haematomas have likewise been described.[10,11] Furthermore, case reports describe severe rectal bleeding more than two weeks after prostate biopsy requiring endoscopic haemostatic treatment.[12] Severe rectal bleeding is thus an uncommon but potentially life-threatening complication and one of which both patients and practitioners should be aware.[13] Post biopsy rectal bleeding is most commonly just a Clavien-Dindo Grade I complication but as outlined above, on occasion, it can result in grade II (eg: blood transfusion required)-IV (organ dysfunction and ICU management) sequelae.

Transperineal (TP) and MRI-fusion biopsies are emerging as alternatives to TRUS biopsy but they have not yet replaced TRUS biopsy due to their increased costs, requirement for general anaesthesia (GA) and lack of widespread availability. In the case of TP biopsies, in one study, a haemorrhagic complication of any type occurred in just 1.8% of cases and none were reported as severe.[14] A comparative study of TRUS biopsy versus TP biopsy showed remarkably greater incidence rates of post-biopsy rectal bleeding (50.5% vs 3.4%, P >0.01) in the former group.[15] MRI-guided prostate biopsy appears to offer no advantage over traditional TRUS biopsy in terms of incidence and duration of bleeding complications.[16] The prostate and surrounding rectal tissue are supplied by a rich vascular network consisting of branches of the Inferior Vesical Artery and the Superior (SRA), Middle (MRA) and Inferior Rectal (IRA) arteries. The rectal venous plexus is also dense in the submucosal space of this region. Specifically, reports suggest that it may be the SRA and MRA that bleed after biopsy.[13,17] Other reports suggest it is the rectal venous plexus which bleeds.[18] Regardless of the precise bleeding source, the anterior rectal wall is classically the location of the

haemorrhage.[8,19] Baum et al. contend that rectal bleeding occurs every 15 minutes as the ampulla fills with blood stimulating the urge to evacuate.[20]

This review examines rectal bleeding post TRUS-guided prostate biopsy. We explore the literature to evaluate risk factors (RFs) for its development and techniques aimed primarily at managing but also preventing this infrequent but occasionally very significant complication.

Methods

A Pubmed literature search was conducted using the keywords "transrectal-prostate-biopsy-bleed". This search yielded 144 "hits" going back to 1970. 62 of these were immediately dismissed as they weren't directly relevant to our review topic. Not all of the 82 papers that were reviewed were ultimately included in our bibliography as some merely echoed what other papers had reported while others added little. A manual search of the bibliography of reviewed studies was also conducted. Additional papers in non-Pubmed listed journals of which the authors were aware were also appraised. Published guidelines from the EAU were included in the literature search process. We also included an "epidemiological" paper which looked at a classification system for surgical techniques. In all, 135 papers were reviewed. 68 are cited in our bibliography– see Figure 1. Eight papers provide level I evidence and two provide level IV evidence. All others provide level II or III evidence - see Table 1. Importantly, there is no consistent or specific definition for what constitutes "severe" or "massive" or "life-threatening" bleeding but haemodynamic instability and the need for blood transfusion were taken as evidence of such bleeding. To the best of our knowledge, this is the first comprehensive review paper looking specifically at post-TRUS biopsy rectal bleeding.

Results

Risk factors (RFs)

Several modifiable RFs which may increase the likelihood of post-TRUS biopsy rectal bleeding have been described.

Anticoagulants/antiplatelets (see Table 2)

Much attention has understandably focused on the widespread use of anticoagulant and antiplatelet agents, with Aspirin being the most ubiquitous of these and thus the most comprehensively studied. Definitive guidelines regarding the management of these medications before a TRUS biopsy are yet to be established. One study reports that nearly 60% of consultant members of the British Association of Urological Surgeons will continue Aspirin prior to a TRUS-guided prostate biopsy while only 8% will continue Clopidogrel and 5% will continue Warfarin.[21] Some studies suggest that patients taking Aspirin have a significantly higher cumulative incidence of rectal bleeding, though these are considered only minor bleeding complications.[22,23] Conversely, others argue that Aspirin does not increase the incidence of rectal bleeding and that Aspirin does not need to be discontinued beforehand.[24]

In Carmignani's meta-analysis, the occurrence of rectal bleeding was not statistically increased in patients taking Aspirin and so it was concluded that stopping Aspirin before TRUS biopsy is unnecessary.[25] Another meta-analysis concluded that low-dose Aspirin neither increases the level of the severity of bleeding complications nor the perioperative mortality because of bleeding complications while discontinuing it increases perioperative cardiovascular risks with life threatening sequelae.[26] In a review paper by the American Urological Association on anticoagulation and antiplatelet therapy in Urological practice, the authors conclude that uninterrupted use of Aspirin does not increase the risk of rectal bleeding after TRUS biopsy.[27] Thus, they recommend continuing Aspirin for patients with moderate/high thromboembolic risks.

Less information is available regarding those taking Clopidogrel or Warfarin. In one of the few studies published, the frequency and severity of bleeding complications were no worse in the Warfarin group than in the control group and the authors concluded that its discontinuation before prostate biopsy may again be unnecessary.[28] Similarly, Halliwell et al. contend that the theoretical risk of a life-threatening bleeding complication in the patient group taking Warfarin is outweighed by the risk of cardio- and cerebro-vascular accidents (CVA) with the cessation of the medication.[29] The risk of CVA with a subtherapeutic INR is estimated to be 0.003%-0.005% per day.[30]

Raheem et al. looked at anticoagulants and antiplatelets as a combined group and concluded that it is unnecessary to cease these agents before TRUS biopsy.[31] A total of 91 and 98 patients were included in their anticoagulation/antiplatelet (monotherapy of Aspirin, Warfarin, Clopidogrel, or Low Molecular Weight Heparin or dual therapy of Aspirin and Warfarin or Clopidogrel) and control groups, respectively. The median INR for Warfarin patients was 2.35. Using a 12-core peripheral zone technique, the authors found the incidence of rectal bleeding to be similar in those taking ≤ two anticoagulants (40%) and those taking none (39%). Little has yet been reported about the effect of new oral anticoagulants (NOACs) on prostate biopsy bleeding rates although one study does recommend discontinuing such agents five days pre-biopsy, bridging with therapeutic Heparin and then restarting the NOAC 6-8 hours after biopsy in the absence of worrisome bleeding.[32]
Interestingly, Asano et al. report no statistical difference with regard to the incidence of rectal bleeding following TP prostate biopsy between those taking antithrombotic agents and those not.[14]

Antibiotics
Prophylactic antibiotics are routinely prescribed pre-biopsy. The Quinolones (especially Ciprofloxacin) are most commonly used as they have good pathogen coverage and excellent prostate penetration. Common alternatives are Co-trimoxazole, Cephalosporins, and Metronidazole. All of these antibiotics facilitate the action of Warfarin and this is another important factor which practitioners must consider when prescribing perioperative Warfarin.[33]

Core biopsy number

According to the literature, the incidence of rectal bleeding following TRUS biopsy varies from 1.3%-58.6%, with a statistically significant positive correlation to the number of core samples obtained.[34] Specifically, rectal bleeding is significantly more prevalent in 12-core prostate biopsy groups than six-core groups; 12-core biopsies at a minimum are now considered the gold standard, with six-core biopsies deemed insufficient for whole gland sampling.[35,36,37]

Local anaesthetic

Debate exists as to the benefit of local anaesthetic (LA) administration with regards to post-biopsy rectal bleeding. Some argue that LA does not reduce the risk whereas other groups contend that LA is associated with a decreased incidence of this complication, presumably due to decreased patient discomfort and less patient movement.[35,38] The addition of Epinephrine to Xylocaine anaesthetic solution diminished the incidence of rectal bleeding in one study.[39]

Other RFs

Other RFs for post-biopsy rectal haemorrhage include the presence of haemorrhoids.[40] The aforementioned rectal venous plexus can increase in size in cases of haemorrhoids.[41] Some authors advise preliminary proctoscopy if haemorrhoids are suspected. Sheikh et al. recommend a TP rather than a transrectal biopsy in patients with severe haemorrhoids.[42] Rietbergen et al. reported an increasing trend of rectal bleeding with advancing age.[43] Poorly controlled hypertension and constipation have also been mooted as potential RFs which should be corrected prior to the procedure.[44] The same authors propose that neovascularization related to large volume, high grade PCa may also contribute to excessive bleeding. Specifically, hypoechoic areas in the prostate are usually hypervascular – biopsying these areas might be an additional RF for bleeding but the dilemma is that these are the precise areas most in need of sampling.[45]

Management

We classified the papers in the below management section according to McCulloch's descriptive model for surgical procedures/techniques delineating stages of Innovation, Development, Exploration, Assessment, and Long-term study (the IDEAL model).[46] To the best of our knowledge, one paper meets the criteria for the Development stage, three papers meet the criteria for the Exploration phase, one paper meets the criteria for the Assessment stage while all others fall into the Innovation phase.

Conservative measures

As with any form of bleeding, initial management of massive post-TRUS biopsy rectal bleeding starts with resuscitation according to Advanced Life Support protocols and blood transfusion may be necessary.[44] Rectal bleeding is traditionally managed with tamponade as the first conservative method. Digital compression of rectal bleeding can be successful in controlling bleeding.[44] Rectal packs may be left in situ for a few hours and removed slowly

after the bleeding has abated.[45] Tamponade by means of a transrectally inserted urethral catheter (UC), tampon or condom is also well described in tackling rectal bleeding post-biopsy.[40,45,47,48] These are left in situ until bleeding stops – this is typically 30-60 minutes in the case of tampons.[48] The normal rectal tone holds these devices against the anterior rectal wall. One such technique involved a 28Fr Foley UC passed through a rectal sponge and inserted with finger-guidance into the rectum - the UC balloon was inflated with 20ml of water to provide effective tamponade.[49] Baum's UC technique involves putting the patient in the supine position, passing a UC per rectum and inflating it with 45mls of water before connecting it to straight drainage.[20] Traction is applied for 45 minutes with the UC taped to the inner thigh. The extent of bleeding can be observed by viewing the contents of the drainage bag.

Even bigger, 60ml balloon three-way UCs have been described.[47] Still, some authors contest that Foley UC balloons are not large enough to be appropriately placed over the bleeding site. The condom balloon tamponade was first reported by Gonen et al. in 2004 - 200mls of water was used to inflate this for two hours.[45] This device was made by inserting a UC into a condom, which was fixed to the UC with sterile silk. The condom balloon tamponade is larger than the Foley balloon tamponade and is easily placed over the bleeding site.[45] Recently, Laracy et al. reported the use of thrombin gel to achieve haemostasis after large volume rectal bleeding.[50]

One method of attempting to prophylactically lower the rate of bleeding involves the insertion of a Foley UC into the rectum with inflation of the balloon to 50cc after biopsy. This has previously been shown to significantly reduce bleeding per rectum from 17.7% in the control group (UC inserted but balloon not inflated) to 1.5% in the non-control group.[51] More recently, the insertion of a gelatin sponge into the rectum after biopsy increased haemostasis without increasing patient symptoms.[52] Park et al. compared TRUS-guided compression on bleeding biopsy tracts immediately after prostate biopsy versus a non-compression group and found that rectal bleeding incidence was significantly lower in the compression group.[53]

Endoscopic correction

Failure of a conservative approach usually mandates an endoscopic attempt at haemostasis. Indeed, early consultation with a Gastroenterologist/Colorectal surgeon with colonoscopic experience is strongly advised. Endoscopic haemostatic measures represent a safe and efficient method to control serious rectal bleeding. Sclerotherapy has been used to successfully treat life-threatening rectal bleeding and is well described.[54] Endoscopic injection of Adrenaline has traditionally been the next management step after unsuccessful conservative measures, with doses of 25 ml of 1:10,000 Adrenaline solution reported.[55] Another sclerosing agent Polidocanol also has been injected successfully.[8] In Brullet's case series of 550 consecutive patients, five (1%) presented with rectal bleeding and hypovolaemic symptoms shortly after TRUS biopsy.[8] Endoscopic injection of Adrenaline and Polidocanol achieved control of bleeding and permanent haemostasis in all. Similarly, endoscopic haemostasis with 1% Athexysclerol has been achieved.[19]

Endoscopic banding has been deployed successfully.[56,57] The bleeding point is controlled with artery forceps passed through the ring of the banding device, with the band mounted ready for application. After the band has been fired, the artery forceps are released. The band remains in situ, securing the haemostasis and sloughing off a few days later.[57] The placement of endoscopic clips is now used in some centres – see Figure 2.[41] Use of endoclipping has been widely reported in Gastrointestinal endoscopy for many years and so this is a potentially promising option for the management of TRUS-biopsy rectal bleeding.[58] Endoclips dislodge spontaneously and are passed in the faeces without complication.[41] Endoscopic thermocoagulation using a 10F multipolar probe with five pulses of two to four seconds each is another method described to stop rectal bleeding.[59] Similarly, both Arroja and Geraci report successful treatment of a major post-biopsy bleed with argon plasma coagulation.[60,61]

Arterial embolization

Historically, pelvic urological embolization consisted of Internal Iliac Artery embolization for uncontrollable haemorrhage from prostate and bladder malignancies.[62] More recently, prostatic arterial embolization for benign prostatic hyperplasia has been tried.[63] In the emergency setting, angiographic embolization has been performed to address catastrophic bleeding post-TRUS biopsy in patients deemed too unstable for colonoscopy. [64,65] It is considered to be fast, safe and accurate. The SRA was the source of bleeding in the former paper, believed to be the first reported case of severe life threatening rectal bleeding following TRUS-guided prostate biopsy effectively managed by angiographic therapy. Elsewhere, selective arterial embolization has successfully resulted in haemostasis of a large pelvic haematoma after biopsy.[66] Additionally, De Beule et al. report a rare case of a post-biopsy prostate arteriovenous fistula resulting in massive rectal haemorrhage which required embolization with calibrated microparticles and microcoils after medical and endoscopic interventions had failed (see Figure 3).[67] Elsewhere, intra-arterial embolization with Gianturco-Wallace coils was performed on a post-biopsy pulsatile perineal haematoma due to a pseudoaneurysm of the Left Hypogastric Artery.[68]

Surgical manoeuvres

GA and transrectal surgical correction of bleeding - oversewing of rectal bleeding points +/- packing of the rectum with Gelfoam - has been reported as an option.[13] This may be performed by dilating the anus with a Parke's retractor and suturing bleeding points in the rectal wall with a 3/0 Vicryl suture. In the above case report, this technique was reported as successful when rectal tamponade with a UC, colonoscopy and angiography had all failed to control the bleeding site. However, it's equally important to consider surgical correction as a viable upfront option, depending on resources and circumstances, and not merely a last resort when other techniques have failed.

Conclusion

TRUS-guided prostate biopsy has become a common procedure since the advent of PSA testing. Rectal bleeding is acknowledged as one of its common side effects. While this is usually mild and self-limiting, it can potentially be deadly. Debate exists as to the risk presented by anticoagulant/antiplatelet use at the time of biopsy although overall, the evidence appears to favour continuing such medications. Other RFs are also well described. Patients and practitioners need to be aware of the RFs for the development of rectal bleeding following prostate biopsy, the potential severity of such bleeding and most importantly, the appropriate measures required to manage it. We advocate early consultation with the Colorectal/Gastroenterology and Interventional Radiology services and a progressive, stepwise approach to its management, starting with resuscitation and conservative tamponade measures, moving to endoscopic haemostasis (injection/banding/clipping) +/- radiological (embolization) +/- transanal surgical methods depending on the clinical scenario, available resources, practitioner preference and success of previous attempted corrective measures (see Figure 4).

Major rectal bleeding post TRUS biopsy is a rare occurrence. This is reflected by the fact that most of the cited papers in our study are case reports, compatible with McCulloch's Innovation phase.[46] To enhance our experience and expertise in managing it, Urologists should be encouraged to report cases of this complication. To facilitate this, centralised registries could be established to capture all such data and a blame-free culture of open reporting needs to be fostered. Future research might also give us a greater understanding and knowledge on the topic. For example, this might include more/larger prospective, randomized controlled trials comparing continued anticoagulation versus no anticoagulation versus withheld anticoagulation, with particular emphasis on the role of NOACs. In addition, studies comparing the efficacy, cost and morbidity of endoscopic versus angiographic management would be of great interest.

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Figures and Tables

Fig. 1. Prisma flow chart outlining accrual of papers for inclusion in our review article.

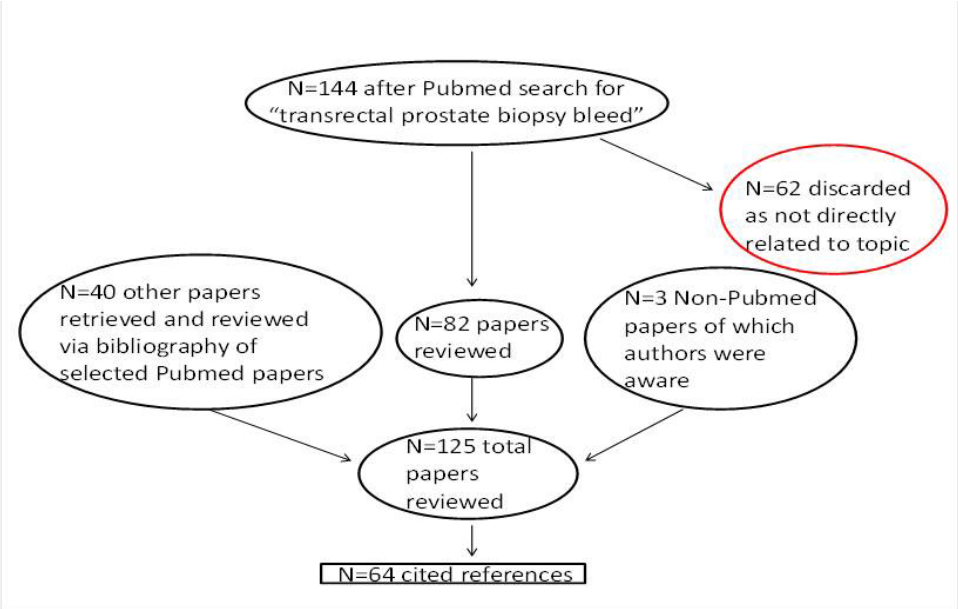
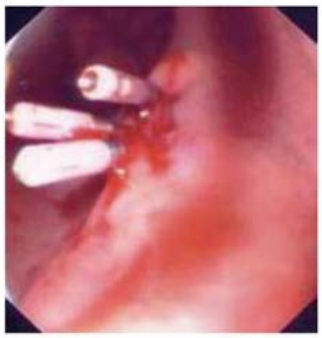


Fig. 2. Images of endoscopic clipping of anterior rectal wall bleeding post-transrectal ultrasound (TRUS) prostate biopsy (reproduced with permission of authors)



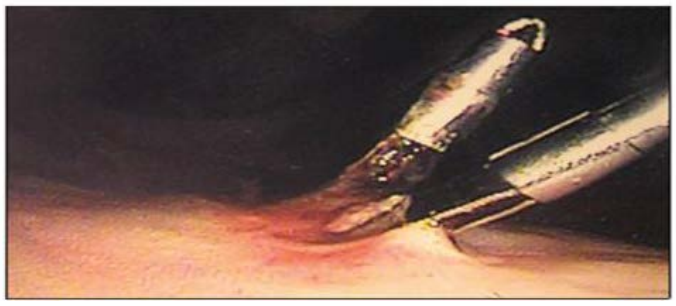


Fig. 3. Control angiography after embolization with microparticles (300–500 μ) and proximal microcoil (arrows) occlusion of the anastomosis of the left and right inferior prostatic arteries (reproduced with permission of author).

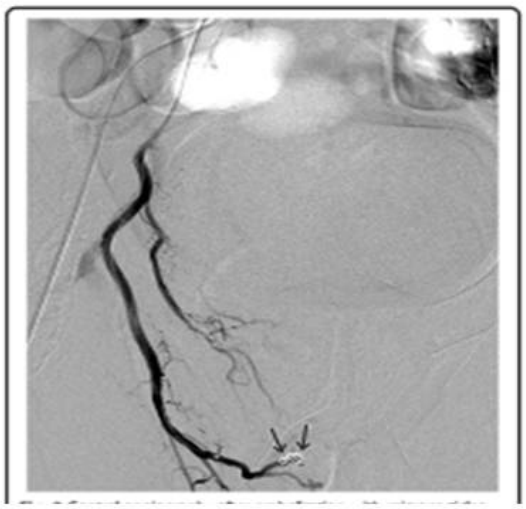


Fig. 4. Proposed hierarchical treatment algorithm for the management of post- transrectal ultrasound (TRUS) biopsy rectal bleeding.

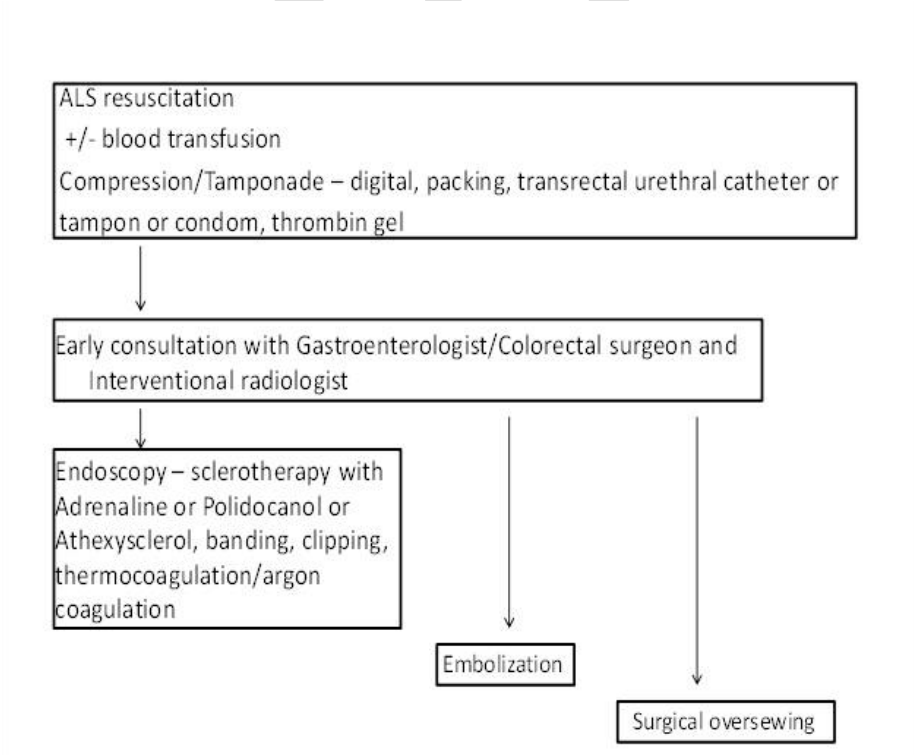


Table 1. Levels of evidence as used in our study	
Ia	Meta-analysis of randomized trials
Ib	≥1 randomized trial
2a	Well-designed, controlled study without randomization
2b	Well-designed, quasi-experimental study
3	Non-experimental study (comparative, correlation, case reports)
4	Expert committee/opinion

Table 2. Selected studies of bleeding complications after prostate biopsy			
First author	**Intervention**	**No. of patients**	**Rectal bleeding %**
Halliwell	ASA vs. nil	387 vs. 731	21 vs. 13
Maan	LDASA vs. nil	36 vs.141	0 vs. 22
Ihezue	Warfarin vs.nil	49 vs. 902	14.3 vs. 13
Raheem	LDASA, warfarin, slopidogrel, LMWH vs. nil	91 vs.98	40 vs. 39
Asano*	ASA, clopidogrel, warfarin, ticlopidine, cilostazol vs. nil	84 vs. 84	0 vs. 0

*Transperineal prostate biopsy. ASA: acetylsalicylic acid; LDASA: low dose acetylsalicylic acid; LMWH: low molecular weight heparin.