Different patterns of postoperative bleeding following cytoreductive surgery for gynecological cancer

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Summary

Purpose of investigation: To study the possible causes of postoperative bleeding following maximal cytoreductive surgery for gynecological cancers.

Method: We have retrospectively reviewed all our cases of postoperative bleeding following major abdominal and pelvic cytoreductive surgery within a 48-hour period. In the postoperative period, replacement therapy was ineffective in achieving hemodynamic stability. During re-operation, the entire abdominal cavity was evaluated for bleeding sites that were adequately ligated or electrocoagulated.

Results: Of 942 women undergoing major cytoreductive surgery 22 women (2.3%) were re-operated for postoperative bleeding after a mean of 14.2 hours. Bleeding was either localized from a vessel in 9 women (40.9%) or diffuse (capillary oozing) in 13 women (59.1). Operative deaths have been as high as 36.8%.

Conclusion: Postoperative bleeding following cytoreductive surgery can be from a single group of vessels or a capillary oozing from the edges or denuded areas of excised peritoneum.

Key words: Cytoreductive surgery; Postoperative hemorrhage.

Introduction

In gynecological oncology, an extensive surgical approach is often necessary when dealing with advanced or recurrent gynecological cancer (cervical, endometrial, sarcomatous and ovarian) as these usually spread throughout the entire pelvic and abdominal cavity and require multiple organ resections and wide peritonectomy to achieve maximal cytoreduction. These extensive surgical procedures can lead to troublesome drawbacks such as intraoperative and postoperative hemorrhage. Some authors have reported a few cases of hemorrhage from lateral pelvic side-wall vessels [1] or from visceral pelvic arteries and retroperitoneal vessels [2-3] when dealing with benign conditions or limited cancer. However when abdominal surgery involves large peritoneal stripping or extreme debulking, a substantial number of postoperative laparotomies due to hemorrhage have been reported [4-8].

Therefore, we have analyzed our experience in order to study the different patterns of bleeding following major pelvic and abdominal surgery for gynecological cancers.

Materials and Methods

We have retrospectively reviewed our cases of postoperative hemorrhage following major cytoreductive surgery for gynecological cancer occurring at the Gynecological Oncology Department of "Centro di Riferimento Oncologico" in Aviano (Italy). From January 1991 to March 1999, 942 women underwent major surgery for advanced or recurrent gynecological malignancies, i.e.: 211 advanced ovarian cancers, 290 recurrent ovarian cancers, 81 advanced cervical cancers, 62 recurrent cervical cancers, 89 advanced or recurrent sarcomas, 75 advanced or recurrent endometrial carcinomas, 72 recurrent colon cancers, and 62 other abdominal and pelvic recurrent malignacies (gastric, breast and melanomas).

Major pelvic or abdominal cytoreductive surgery has been defined as surgery for advanced or recurrent gynecological cancers needing excision of large (greater than five centimeters) recurrences, abdominal organ resections, para-aortic lymphadenectomy and large peritonectomies. In previously untreated cases, radical or simple hysterectomies were excluded from our analysis when associated with pelvic lymphadenectomy only; however those cases where lymphadenectomy was extended above the common iliac nodes were included. Explorative laparotomy with no attempt of debulking surgery was also excluded from this analysis. Cases of abdominal or pelvic recurrences from other malignancies (stomach, colon, breast or melanomas) were included instead whenever they required excision of large masses or major surgery as previously defined. From these cases of major pelvic or abdominal surgery, we then selected those which required re-operation within 48 hours due to postoperative hemorrhage not controllable with infusional therapy only.

In our institution, cytoreductive surgery is performed with a long median abdominal incision. In order to first evaluate whether the surgical approach can be successful and consequently can be performed a thorough cytoreduction a wide exposition of the surgical field is achieved. When surgery requires a wide peritonectomy and abdominal or pelvic organ excision, bleeding sites are carefully electrocoagulated and vessels ligated. Abdomen suturing is not performed until an adequate control of hemostasis has been achieved (that is absence of both bleeding from vessels and major oozing from the denuded peritoneal surfaces) and the patient is hemodynamically stable. During surgery crystalloids, colloids and blood are infused through a central venous catheter and the amount is routinely recorded; Swan-Ganz catheterization is not routinely instituted.

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An intra-abdominal or retroperitoneal drainage is put in place after major cytoreductive surgery to monitor postoperative bleeding. In the first postoperative period, every patient is managed in the intensive care unit with continuous monitoring of vital signs (heart rate, blood pressure, central venous pressure) and laboratory data (hemoglobin, hematocrit, platelet count, prothrombin time and partial thromboplastin time, fibrinogen, and serum electrolytes). These data are used to guide the appropriate postoperative fluid and blood replacement. Blood is transfused if hemoglobin value is less than 8 g/100 ml, and fresh frozen plasma if the international normalized ratio of prothrombin time (I.N.R.) is greater than 1.3. If the postoperative crystalloid, plasma expanders and blood component replacement therapy are inefficient in achieving hemodynamic stability then a decision about re-operation is taken.

During re-operation, through the same wide longitudinal incision of the first surgery, a thorough and careful inspection of every bleeding site is accomplished; bleeding is defined as localized when a specific vessel or group of vessels can be identified; ligation is then performed. In case no vessel can be clearly recognized, bleeding is defined as diffuse and electrocoagulation of bleeding surfaces is conducted until accurate hemostasis is obtained. The abdominal incision is then sutured. Each patient is subsequently monitored in the intensive care unit until critical conditions desist; after hospital discharge, the patient is then followed-up for cancer recurrence.

Statistical analysis has been performed with the t-test for unpaired samples; categorical value significance has been tested with the chi-square. Difference was considered significant if $p<0.05$.

Results

Of the 942 women who underwent major surgery for advanced or recurrent gynecological malignancies, 22 (2.3%) had an early re-operation due to postoperative hemorrhage treated with fluid and blood component replacement therapy but without achievement of hemodynamic stability. These patients included: nine advanced ovarian cancers, eight recurrent ovarian cancers, one recurrent and one advanced leiomyosarcoma, one recurrent peritoneal mesothelioma, one recurrent tubal cancer and one recurrent endometrial cancer. Ascites was present in 11 out of 22 women (50%) at the time of first surgery. Mean intervention time of all 22 women was 6 hours (range 4-9). All these women had an ECOG performance status less than 2 before debulking surgery.

Mean intraoperatory fluid losses were 8,500 ml (median 8,700, range 6,000-15,000). Fluid replacement therapy was the following: crystalloid mean 6,256 ml (range 4000-9750), plasma expander mean 1,688 ml (range 500-4000), 3 mean fresh frozen plasma units (range 2-8) and 5 mean blood units (range 2-14). Surgical cytoreduction was complete (no residual disease) in eight women, while tumor was left in 14 women. Surgical procedures performed during the first surgery in these 22 women were: 13 hysterectomies with bilateral adnexectomy, 14 omentectomies, 13 pelvic lymphadenectomies, 11 para-aortic lymphadenectomies, 12 low anterior rectal resections, 3 partial colectomies, 3 ileum resections, 13 wide peritonectomies, 3 splenectomies, 1 liver resection, 3 cholecystectomies, 1 partial bladder resection and 1 ureteric reimplantation.

Re-operation for intractable postoperative bleeding was performed after a mean of 14.2 hours (range 4-48). Localized bleeding was seen in nine women (40.9%), while in 13 (59.1%) there was a diffuse capillary oozing from excised peritoneal surfaces and edges. In the nine women with localized bleeding, it was from retroperitoneal vessels (two women), from gastroepiploic vessels (one woman), from the presacral plexus (one woman), and from the splenic artery (one woman). In the remaining four women who were bleeding from the gastrosplenic ligament, single ligature of vessels was inefficient to relieve bleeding and splenectomy was implemented. In the 13 women with diffuse capillary oozing, it was from various sites of excised peritoneum: pelvic (two women), diaphragmatic (two women), lateral to colon (three women) and multiple sites (six women). The oozing was stopped by electrocoagulation and multiple ligatures of peritoneal edges.

There was no statistical difference between the two groups of localized bleeding and diffuse capillary oozing in the amount of crystalloids (7,350 vs 6,380) ml), plasma expanders (1,880 vs 1,920 ml), and blood (4.7 vs 5.7 units) infused during the first surgery. The time between the first surgery and re-operation (11.3 vs 16.1 hours) was also not statistically significant although a trend toward a shorter interval for localized bleeding was seen.

Of the 13 women in whom large peritonectomies had been performed, six (46.1%) had oozing from the denuded areas of peritoneal surfaces. In the remaining seven women with diffuse oozing, it was from peritoneal edges excised during left colon mobilization (three patients) or removal of large masses (two patients).

As for early complications following re-operation, we observed four fatal Adult Respiratory Distress Syndrome, four enteric fistulas following exenterative surgery, two massive left pleural effusions after splenectomy during re-operation, and one persistent but benign hyperbilirubinemia.

Eight of the 22 women (36.4%) died in the postoperative period, two of the localized bleeding group and six of the diffuse oozing group. Seven women are still alive and free from cancer (after a median of 14 months), four relapsed but they are still alive (median follow-up 19 months) and three died of cancer (median follow-up seven months).

Discussion

Postoperative bleeding following abdominal surgery for gynecological cancer is one of the drawbacks ranging, when reported, from 1 to 12% [5-10].

Aggressive cytoreductive surgery is the surgical option in advanced or recurrent gynecological cancer, usually requiring radical resection of large masses infiltrating the greater omentum, tissues adjacent to the spleen, greater gastric curvature, pancreas, colon and rectum. This is the

reason why a radical omentectomy often has to be extended to the short gastric vessels and to the hilum of the spleen with the possible risk of damaging vessels that will bleed subsequently. Moreover, the dissection of an infiltrated gastrosplenic ligament can lead to capsular avulsion injury of the spleen and resultant bleeding from it either immediately or delayed [7]. In our experience five out of eight localized bleeding were from the previously severed gastrosplenic ligament and in four women splenectomy had to be performed to control postoperative hemorrhage.

In the other cases of localized bleeding it was, in two, from retroperitoneal vessels following para-aortic lymphadenectomy, as described by others [2, 8], in one from the splenic artery following splenectomy, and from the presacral plexus in another where a bulky pelvic mass infiltrating the pelvic wall required severing of the presacral fascia. Indeed, while dissecting a large neoplastic lesion infiltrating the rectum or the posterior pelvic wall, the presacral venous plexus, which lies posteriorly to the fascia propria of the rectum, can be exposed and inadvertently damaged causing bleeding that is usually intraoperative [11, 12]. In fact, we have experienced some intraoperative hemorrhage from this site (usually managed by packing the pelvis with a large gauze subsequently extracted through the vagina in the postoperative period) but only one case of postoperative bleeding requiring re-operation after 22 hours, handled by multiple ligations of the presacral plexus and packing of the pelvis.

Although we have experienced a 40.9% of postoperative hemorrhage from groups of vessels not bleeding at closure of the abdomen, we have also observed a 59.1% of postoperative capillary oozing from denuded peritoneal surfaces stripped away during debulking surgery or from edges of peritoneum cut to either mobilize the colon or excise a large tumoral mass. Such pattern of postoperative hemorrhage was unexpected since in the papers we reviewed [5-9] no mention was made about it although some authors [5, 6] have used large peritonectomy procedures while dubulking cancer spread throughout the abdominal cavity.

It is noteworthy that at the end of every surgical debulking we have performed, all the peritoneal cavity was evaluated for bleeding sites and hemostasis carefully achieved. There are some possible explanations for the unexpected postoperative oozing. Aggressive debulking surgery is time consuming, thus leading to large wasting of biological fluids (all our women had intraoperatory fluid losses greater than 6,000 ml) and increasing both the overall surgical risk and the incidence of morbidity. Moreover, gynecological tumors can release a considerable amount of fibrinolysis activators possibly altering the hemostatic balance *in vivo* [13]. This could explain the delayed diffuse oozing not apparently limited to the patients who had undergone extensive peritonectomy. In fact, almost half the women in this group had only severing of peritoneal edges in order to mobilize the colon or excise a tumoral mass, ruling out the hypothesis that a large denuded and not electrocoagulated subperitoneal area is a prerequisite for diffuse oozing.

We could suggest another interpretation of these diffuse postoperative oozing, not mentioned in other papers. During aggressive debulking surgery, owing to wastage of biological fluid and surgical distress, there can be a relative, not deliberate, hypotension possibly masking small bleeding from the denuded subperitoneal surface or from peritoneal edges. However, during the postoperative period, after the blood pressure returns to normal, there could be a "reactionary hemorrhage" although a careful hemostasis was apparently achieved at the end of the debulking procedure [14]. This could not have been influenced by the technique used to excise the peritoneal surfaces involved by neoplasm. In fact, our technique in excising the peritoneum consists of stripping it bluntly, whereas others [4, 5] use ball-tip electrosurgery to achieve immediate bleeding control; however this does not seem to eliminate postoperative intra-abdominal bleeding.

Conclusion

Postoperative bleeding in cytoreductive abdominal and pelvic cancer surgery seems to be both unavoidable and burdened with severe prognosis. Unavoidable because, even with accurate hemostasis at the end of surgery at least 3% of patients will develop it, and with severe prognosis because operative mortality after re-operation could be as high as one out of three, which is a 1% risk of operative mortality due to postoperative hemorrhage. However, in our opinion, that risk should be taken and balanced with the benefits carried by surgical debulking in gyencological oncology.

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