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Blood salvage and cancer surgery: should we do it?

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In this edition of **TRANSFUSION**,[1] a case series is presented where blood salvage was used during surgery for gynecologic malignancy. Commonly, blood salvage is avoided in cancer surgery due to a fear of creating disseminated metastasis from incorporating cancer cells into the shed blood and reinfusing them directly into circulation. In the case series presented here, diffuse metastasis did not arise shortly thereafter. While a case series does not prove the safety of this technology during oncologic surgery, it does provide an opportunity to review the data regarding this contraindication.

Classically, cancer metastasis has been thought to arise from cells breaking away from a primary tumor, migrating into the blood and landing in distal organs from which a secondary tumor would grow. Based on this understanding, it would seem like a bad idea to collect blood and cancer cells from an operative site and then directly reinfuse them into circulation. In 1975, a case report was published where a patient had blood salvage utilized during a pneumonectomy. Four weeks later, the patient died. Since malignant cells were detected in the salvaged blood, the authors concluded that the reinfusion of these cells was contributory to the patient's early demise.[2] Based on this theoretical fear of creating diffuse metastasis when utilizing blood salvage during cancer surgery, the American Medical Association Council on Scientific Affairs in 1986 recommended against the use of blood salvage during cancer surgery.[3]

Since this recommendation, the alternative therapy to blood salvage, allogeneic transfusion, has been questioned as to its effects on cancer recurrence. Additionally, many other adverse effects associated with allogeneic transfusion such as transfusion-related acute lung injury have been identified. So, a reevaluation of the use of blood salvage during oncologic surgery is warranted.

Since 1986, there have been 10 studies published encompassing 476 patients who received blood salvage during resection of multiple different tumor types involving the liver,[4–6] prostate,[7–9] uterus,[10,11] and urologic system.[12,13] Three of these publications were observational case series like the report in this issue of **TRANSFUSION**. Like the report here, these observational studies did not show diffuse blossoming of metastasis shortly after.

CONFLICT OF INTEREST
None.

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In the other seven of these 10 studies, outcomes in a matching group of patients were reported. These matched controls received no transfusion, allogeneic transfusion, or preoperative autologous donation instead of blood salvage. Patient follow-up in these studies varied from 3 to 10 years. In all of the studies, the blood salvage group received less allogeneic blood than its comparable control. In all circumstances, the long-term outcome was equivalent or better in the blood salvage group when compared to the control. All studies were retrospective in nature so the level of evidence is weak; however, these studies clearly provide no support for the theoretical risk of administering blood containing malignant cells and subsequent widespread metastasis.

Since no outcome data exist supporting the contraindication, are there any data by which we can infer possible risk? The primary question to ask is, “Are cancer cells, which are capable of causing metastasis, present in the blood being retransfused?” The answer to this question appears simple. Besides the case report mentioned at the beginning of this editorial, Catling and colleagues[14] found tumor cells in the blood salvage reservoirs of 31 of 50 patients undergoing gyneco-oncology surgery. In a different report, Hansen and colleagues[15] demonstrated tumor cells in blood salvaged from the surgical field, ranging in quantities from 10 to 10^6 cells. Clearly, the cells are present within the scavenged blood.

Interestingly, Hansen and colleagues also found that in 26% of these patients, there were also tumor cells circulating in the patients that were not from readministered salvaged blood. In fact, it has been demonstrated that a high percentage of patients presenting for cancer surgery have circulating tumor cells.[16–18] Additionally, it has long been recognized that surgical manipulation of the tumor leads to circulatory dissemination of cancer cells.[19–21] It has been estimated that of these circulating tumor cells, only 0.01% to 0.000001% of them have the potential to form metastatic lesions.[22] So, the importance of administration of tumor cells via cell salvage blood must be questioned in light of the fact that they are already there.

If tumor cells are already in circulation, is there any significance to adding a few more? Circulating tumor cells have been associated with poor prognosis in breast[23] and prostate cancer, for which there is an extremely sensitive FDA-licensed test that quantifies cytokeratin-positive cells in blood. Further, for epithelial cancers, the blood is a conduit to metastatic sites such as marrow. Since patients with even micrometastatic marrow involvement have poor prognosis,[24] it follows that at least some circulating tumor cells are tumorigenic. Direct evidence for surgical release of tumor cells into the peripheral blood is available in esophageal cancer, where Liu and coworkers[25] used polymerase chain reaction to quantify tumor cells in the blood of patients undergoing esophagectomy. Patients in whom the level of circulating tumor cells remained elevated 3 days postoperatively had a higher incidence of subsequent metastasis. However, the release of circulating tumor cells correlated with other classical prognostic indicators such as pathologic stage and lymph node status, highlighting the conundrum inherent in these observational studies: it is not possible to tell whether the presence of circulating cells is the cause or consequence of elevated risk. Whether adding tumor cells into the circulation worsens prognosis is a question yet left unanswered.

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Taking the most conservative stance and assuming that circulating tumor cells do have malignant potential, can we remove them from salvaged blood? This issue remains an area of controversy. Leukoreduction filters have been advocated for removal of tumor cells during cancer surgery. These filters have been used for filtration of malignant cells in cell salvage for urologic surgery[26,27] and pulmonary surgery[28] and in a variety of cell lines that were used to contaminate discarded blood.[29,30] These studies have all concluded that leukoreduction filters were highly effective at removing tumor cell contamination. Hansen and coworkers[31] suggest that these studies are flawed in that they are performed with cultured tumor cells that may stick to filter material at greater rates than would cells from the surgical site. He also contends that the assays used for detection of tumor cells in these studies lack sensitivity and that cells may in fact be present in this shed, filtered blood. It is suggested from the work of Hansen and coworkers that a 3- to 4-log reduction in tumor burden is achieved with leukoreduction filters. Thus, he advocates irradiation of the tumor-laden blood utilizing 50 Gy of gamma irradiation. He believes that this achieves a 12-log reduction in tumor cells. While this may be true, most hospital irradiators are programmed to provide smaller doses of radiation, which would complicate the provision of irradiated allogeneic blood; many hospitals do not have these irradiators, meaning that the blood would need to be transported off site to a blood center prolonging the turnaround time for the reinfusion; and, finally, separating the blood from the patient presents new risks of hemolytic transfusion reactions.

Although this debate exists among advocates of either removal technique, it may be irrelevant as to whether either technique is used. Of the seven blood salvage studies mentioned earlier where a control group existed, in six of the seven studies neither removal technique was used. In the seventh article, a leukoreduction filter was used.

The last question to ponder is whether blood salvage offers an alternative that is equivalent or equal to the alternative—allogeneic transfusion. Multiple reports have been made indicating that allogeneic transfusion increases the rates of recurrence after tumor surgery.[32–34] Two recent meta-analyses of these reports suggest that patients suffer nearly a twofold increase in recurrence when exposed to allogeneic transfusion and that the effect is dose-dependent.[35,36] While critics of these studies would state that these studies demonstrate an association between allogeneic blood and tumor recurrence, it is not proven that this relationship indeed exists. Nevertheless, from the prevailing evidence at hand, it would appear that the association of cancer recurrence with allogeneic blood is evidence that has sizably more weight to it than does the theoretical risk of utilizing blood salvage in cancer surgery.

While we await the performance of a prospective, randomized controlled trial to answer the question definitively of the best technique for providing red blood cells during cancer surgery, for now the preponderance of evidence appears to support the use of blood salvage. At this point, the use of leukoreduction filters appears prudent.

References

1. Nagarsheth NP, Sharma T, Shander A, Awan A. Blood salvage use in gynecologic oncology. Transfusion. 10.1111/j.1537-2995.2009.02256.x

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2. Yaw PB, Sentany M, Link WJ, Wahle WM, Glover JL. Tumor cells carried through autotransfusion. Contraindication to intraoperative blood recovery? JAMA. 1975; 231:490–1. [PubMed: 1172829]

3. Autologous blood transfusions. Council on Scientific Affairs. JAMA. 1986; 256:2378–80. [PubMed: 3773142]

4. Hirano T, Yamanaka J, Iimuro Y, Fujimoto J. Long-term safety of autotransfusion during hepatectomy for hepatocellular carcinoma. Surg Today. 2005; 35:1042–6. [PubMed: 16341484]

5. Muscari F, Suc B, Vigouroux D, Duffas JP, Migueres I, Mathieu A, Lavayssiere L, Rostaing L, Fourtanier G. Blood salvage autotransfusion during transplantation for hepatocarcinoma: does it increase the risk of neoplastic recurrence? Transpl Int. 2005; 18:1236–9. [PubMed: 16221153]

6. Zulim RA, Rocco M, Goodnight JE Jr, Smith GJ, Krag DN, Schneider PD. Intraoperative autotransfusion in hepatic resection for malignancy. Is it safe? Arch Surg. 1993; 128:206–11. [PubMed: 8381647]

7. Davis M, Sofer M, Gomez-Marin O, Bruck D, Soloway MS. The use of cell salvage during radical retropubic prostatectomy: does it influence cancer recurrence? BJU Int. 2003; 91:474–6. [PubMed: 12656896]

8. Gray CL, Amling CL, Polston GR, Powell CR, Kane CJ. Intraoperative cell salvage in radical retropubic prostatectomy. Urology. 2001; 58:740–5. [PubMed: 11711352]

9. Stoffel JT, Topjian L, Libertino JA. Analysis of peripheral blood for prostate cells after autologous transfusion given during radical prostatectomy. BJU Int. 2005; 96:313–5. [PubMed: 16042720]

10. Mirhashemi R, Averette HE, Deepika K, Estape R, Angioli R, Martin J, Rodriguez M, Penalver MA. The impact of intraoperative autologous blood transfusion during type III radical hysterectomy for early-stage cervical cancer. Am J Obstet Gynecol. 1999; 181:1310–5. [PubMed: 10601905]

11. Connor JP, Morris PC, Alagoz T, Anderson B, Bottles K, Buller RE. Intraoperative autologous blood collection and autotransfusion in the surgical management of early cancers of the uterine cervix. Obstet Gynecol. 1995; 86:373–8. [PubMed: 7651645]

12. Klimberg I, Sirois R, Wajsman Z, Baker J. Intraoperative autotransfusion in urologic oncology. Arch Surg. 1986; 121:1326–9. [PubMed: 3778206]

13. Hart OJ 3rd, Klimberg IW, Wajsman Z, Baker J. Intraoperative autotransfusion in radical cystectomy for carcinoma of the bladder. Surg Gynecol Obstet. 1989; 168:302–6. [PubMed: 2928904]

14. Catling S, Williams S, Freites O, Rees M, Davies C, Hopkins L. Use of leucocyte filter to remove tumour cells from intraoperative cell salvage blood. Anaesthesia. 2008; 63:1332–8. [PubMed: 19032302]

15. Hansen E, Wolff N, Knuechel R, Ruschoff J, Hofstaedter F, Taeger K. Tumor cells in blood shed from the surgical field. Arch Surg. 1995; 130:387–93. [PubMed: 7710337]

16. Klimberg IW. Autotransfusion and blood conservation in urologic oncology. Sem Surgical Oncology. 1989; 5:286–92.

17. Salsbury AJ. The significance of the circulating cancer cell. Cancer Treatment Reviews. 1975; 2:55–72. [PubMed: 1102085]

18. Cole WH. The mechanisms of spread of cancer. Surg Gynecol Obstet. 1973; 137:853–71. [PubMed: 4594179]

19. Oefelein MG, Kaul K, Herz B, Blum MD, Holland JM, Keeler TC, Cook WA, Ignatoff JM. Molecular detection of prostate epithelial cells from the surgical field and peripheral circulation during radical prostatectomy. J Urol. 1996; 155:238–42. [PubMed: 7490843]

20. Roberts S, Watne A, McGrath R, McDrew E, Cole W. Technique and results of isolation of cancer cells from the circulating blood. Arch Surg. 1958; 76:334–6.

21. Fisher ER, Turnbull RB Jr. Cytologic demonstration and significance of tumor cells in the mesenteric venous blood in patients with colorectal carcinoma. Surg Gynec Obstet. 1955; 100:102–5. [PubMed: 13238159]

22. Weiss L. Metastatic inefficiency: causes and consequences. Cancer Rev. 1986; 3:1–24.

23. Cristofanilli M, Budd GT, Ellis MJ, Stopeck A, Matera J, Miller MC, Reuben JM, Doyle GV, Allard WJ, Terstappen LW, Hayes DF. Circulating tumor cells, disease progression, and survival in metastatic breast cancer. N Engl J Med. 2004; 351:781–91. [PubMed: 15317891]

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24. Pantel K, Brakenhoff RH, Brandt B. Detection, clinical relevance and specific biological properties of disseminating tumour cells. Nat Rev Cancer. 2008; 8:329–40. [PubMed: 18404148]
25. Liu Z, Jiang M, Zhao J, Ju H. Circulating tumor cells in perioperative esophageal cancer patients: quantitative assay system and potential clinical utility. Clin Cancer Res. 2007; 13:2992–7. [PubMed: 17505001]
26. Edelman MJ, Potter P, Mahaffey KG, Frink R, Leidich RB. The potential for reintroduction of tumor cells during intraoperative blood salvage: reduction of risk with use of the RC-400 leukocyte depletion filter. Urology. 1996; 47:179–81. [PubMed: 8607229]
27. Wiesel M, Gudemann C, Hoever KH, Staehler G, Martin E. Separation of urologic tumor cells from red blood cells by the use of a cell-saver and membrane filters. Investig Urol. 1994; 5:244–8.
28. Perseghin P, Vigano M, Rocco G, Della Pona C, Buscemi A, Rizzi A. Effectiveness of leukocyte filters in reducing tumor cell contamination after intraoperative blood salvage in lung cancer patients. Vox Sang. 1997; 72:221–4. [PubMed: 9228711]
29. Kongsgaard UE, Wang MY, Kvalheim G. Leucocyte depletion filter removes cancer cells in human blood. Acta Anaesthesiol Scand. 1996; 40:118–20. [PubMed: 8904269]
30. Torre GC, Ferrari M, Favre A, Razzetta F, Borgonovo G. A new technique for intraoperative blood recovery in the cancer patient. Eur J Surg Oncol. 1994; 20:565–70. [PubMed: 7926061]
31. Hansen E, Knuechel R, Altmeppen J, Taeger K. Blood irradiation for intraoperative autotransfusion in cancer surgery: demonstration of efficient elimination of contaminating tumor cells. Transfusion. 1999; 39:608–15. [PubMed: 10378841]
32. Francis DM. Relationship between blood transfusion and tumour behaviour. Br J Surg. 1991; 78:1420–8. [PubMed: 1773314]
33. Vamvakas EC. Perioperative blood transfusion and cancer recurrence: meta-analysis for explanation. Transfusion. 1995; 35:760–8. [PubMed: 7570938]
34. Blumberg N, Heal JM. Effects of transfusion on immune function. Cancer recurrence and infection. Arch Pathol Lab Med. 1994; 118:371–9. [PubMed: 8166587]
35. Vamvakas EC. Perioperative blood transfusion and cancer recurrence: meta-analysis for explanation. Transfusion. 1995; 35:760–8. [PubMed: 7570938]
36. Amato AC, Pescatori M. Effect of perioperative blood transfusions on recurrence of colorectal cancer: meta-analysis stratified on risk factors. Dis Colon Rectum. 1998; 41:570–85. [PubMed: 9593238]