Bölüm
54

PANKREAS CERRAHİSİ UYGULANACAK HASTALARIN ANESTEZİ YÖNETİMİ

Evrim KUCUR TÜLÜBAŞ[64]

GİRİŞ

Pankreas kanseri (PC), kansere bağlı ölüm nedenleri içinde altıncı sıradadır ve dünyadaki hayatta kalma oranı en düşük hastalıktır (1). En ölümcül sindirim sistemi kanseri türüdür. Evreleme ve yerleşim yerine göre beş yıllık hayatta kalma oranı % 5'dir. Bu son derece kötü prognozun başlıca nedeni, hastaların %15'inden daha azında rezektabl tümör teşhisi konmasıdır(2). Günümüzde, PC için tek küratif tedavi, cerrahi rezeksiyondur; ancak rezeke edilebilir tümörler için bile kür halen nadirdir (5 yıllık yaşama oranı yaklaşık% 15-% 20) (3).

Cerrahi komplikasyonlardan çok, sistemik hastalıklar PC ile ilişkili ölümlerin çoğuna neden olmaktadır (4). PC'lerin % 80'inden fazlası 65 yaş üstünde görülmektedir. Pek çok PC hastası yoğun sigara içicisidir veya geçmişte sigara içmiştir (5,6) ve PC hastalarının neredeyse% 80'inde ya diyabet ya da bozulmuş glikoz toleransı (7) mevcuttur. Major komplikasyon olarak venöz tromboembolizm gelişebilir (8). Bu nedenlerden dolayı, PC gibi major abdominal cerrahi ameliyatı geçirecek hastalar, anestezi risk sınflandırmasında yüksek risk grubundadır. Bu hastaları genel sonucu iyileştirmek için multidisipliner bir yaklaşımın uygulandığı ve deneyimli ekiplerin çalıştığı yüksek işlem hacmine sahip merkezlere yönlendirmek önemlidir. Ayrıca, dikkatli hasta seçimi esastır. Hastaların morbiditesi, hasta sınıflandırma ve seçiminden başlayarak, anestezi yönetiminden (Tablo 1), cerrahi olarak yapılan işlemlerden, postoperatif yoğun bakım ünitesindeki tedavisinden önemli ölçüde etkilenir.

Tablo 1. Pankreas kanseri için ameliyat olacak hastaların perioperatif yönetimi

Ameliyat öncesi
- Bilgilendirilmiş hasta onayı preoperatif risk değerlendirmesi
- Preoperatif fiziksel durumların ve ilaçların değerlendirilmesi ve optimizasyonu
- Beslenme durumu
- Risk sınıflaması
- Tromboprofilaksi için gerekçe ve öneriler

Ameliyat
- Kombine genel ve epidural analjezi
- Cerrahi alan enfeksiyonunun önlenmesi
- Antimikrobiyal profilaksi
- Hipotermiden kaçının
- Glikoz kontrolü
- Kan transfüzyonu yönetimi
- İntraoperatif sıvı yönetimi
- İntraoperatif ventilasyonun optimizasyonu
- İntraoperatif tromboprofilaksi

Ameliyat Sonrası
- Erken nazogastrik tüp, kateter ve drenaj çekilmesi
- Erken oral beslenme / glisemik kontrol / hedefe yönelik sıvı tedavisi
- Ağrı kesici / opioid olmayan oral analjezi
- Postoperatif ve venöz tromboembolik önleme yoğun solunum rehabilitasyonu
- Postoperatif yoğun yönetimi

[64] Uzman Doktor, SBÜ İstanbul Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Anestezi ve Reanimasyon Kliniği, evrim.kucurtulubas@saglik.gov.tr

nün yeterli bir süre olabileceğini düşünmekteyiz. İntravenöz opioidleri kullanan hasta kontrollü analjezi, aynı etkin analjezi sağlamaz ve lokal epidural anestezik tekniklere kıyasla cerrahi stres yanıtları üzerinde daha az faydalı fizyolojik etkiler ortaya çıkarır (129).

Venöz Tromboembolinin Önlenmesi

Erken mobilizasyon alt ekstremite derin venöz tromboz riskini ve pulmoner komplikasyonları azaltabilir (130). Bu hasta popülasyonunda özellikle yüksek olan VTE riski, preoperatif dönemin başlangıcından itibaren yönetilmeli, erken mobilizasyon ve uygun farmakolojik tromboprofilaksi sonucu postoperatif döneme kadar tüm cerrahi operasyon sırasında devam etmelidir.

Solunum Rehabilitasyonu

Pankreas rezeksiyonu sonrası pulmoner komplikasyonlar tüm hastaların yaklaşık dörtte birinde görülür (131). Anestezi altında ve / veya ameliyat sonrası meydana gelen birçok patofizyolojik modifikasyon, birbirleriyle etkileşime girerek solunum komplikasyonlarına neden olabilir. Ameliyat sonrası pulmoner disfonksiyonun temel nedenlerinden biri atelektazidir (132).

Üst abdominal ve torasik cerrahi sonrası, solunum komplikasyonlarının ve atelektazinin önemli bir belirleyicisi olan postoperatif diyafragma disfonksiyonu (133) sıklıkla gözlenir.

Son yıllarda akciğer komplikasyonlarını önlemek için preoperatif dönemde solunum egzersizleri önerilmektedir. Sistematik bir gözden geçirme, postoperatif non-invaziv ventilasyonun, özellikle sürekli pozitif solunum yolu basıncının (CPAP), abdominal cerrahi geçiren hastalarda hem postoperatif komplikasyonları hem de entübasyon gereksinimini azalttığını göstermiştir (130)

Yoğun Postoperatif Yönetim

Ameliyat tekniğinde ve perioperatif yönetimde sürekli gelişen yöntemlere rağmen, büyük abdominal cerrahi uygulanan hastaların artan yaş nedeni ile morbidite, mortalite, hastanede kalış süresi ve hastane maliyetlerinde artışa yol açar. Pankreatikoduodnektomi sonrası postoperatif yan etki oranının yaklaşık %20'dir (134). Bu nedenlerden dolayı pankreas kanseri ameliyatları geçiren hastaları postoperatif yoğun bakım ünitesinde (YBÜ) takip etmek gereklidir. Bu sayede hedefe yönelik sıvı terapisi, invaziv ve non-invaziv ventilasyon olasılığı, intravenöz ilaçların sürekli uygulanması ve yakın hemodinamik izlem sağlanabilmektedir.

KAYNAKLAR

1 Michaud DS. Epidemiology of pancreatic cancer. *Minerva Chir* 2004; 59: 99-111 (PMID: 15238885)

2 Kedra B, Popiela T, Sierzega M, Precht A. Prognostic factors of long-term survival after resective procedures for pancre-atic cancer. *Hepatogastroenterology* 2001; 48: 1762-1766 (PMID:11813619)

3 Kosuri K, Muscarella P, Bekaii-Saab TS. Updates and con-troversies in the treatment of pancreatic cancer. *Clin Adv Hematol Oncol* 2006; 4: 47-54 (PMID: 16562370)

4 Marandola M, Cilli T, Alessandri F, Tellan G, Caronna R, Chirletti P, Delogu G. Perioperative management in patients undergoing pancreatic surgery: the anesthesiologist's point of view. *Transplant Proc* 2008; 40: 1195-1199 (PMID: 18555147 DOI: 10.1016/j.transproceed.2008.03.114)

5 Lynch SM, Vrieling A, Lubin JH, Kraft P, Mendelsohn JB, Hartge P, Canzian F, Steplowski E, Arslan AA, Gross M, Helzlsouer K, Jacobs EJ, LaCroix A, Petersen G, Zheng W, Albanes D, Amundadottir L, Bingham SA, Boffetta P, Boutron-Ruault MC, Chanock SJ, Clipp S, Hoover RN, Ja-cobs K, Johnson KC, Kooperberg C, Luo J, Messina C, Palli D, Patel AV, Riboli E, Shu XO, Rodriguez Suarez L, Thomas G, Tjønneland A, Tobias GS, Tong E, Trichopoulos D, Virtamo J, Ye W, Yu K, Zeleniuch-Jacquette A, Bueno-de-Mesquita HB, Stolzenberg-Solomon RZ. Cigarette smoking and pan-creatic cancer: a pooled analysis from the pancreatic cancer cohort consortium. *Am J Epidemiol* 2009; 170: 403-413 (PMID: 19561064 DOI: 10.1093/aje/kwp134)

6 Brand RE, Greer JB, Zolotarevsky E, Brand R, Du H, Sime-one D, Zisman A, Gorchow A, Lee SY, Roy HK, Anderson MA. Pancreatic cancer patients who smoke and drink are diagnosed at younger ages. *Clin Gastroenterol Hepatol* 2009; 7: 1007-1012 (PMID: 19560558 DOI: 10.1016/j.cgh.2009.06.008)

7 Permert J, Ihse I, Jorfeldt L, von Schenck H, Arnqvist HJ, Larsson J. Pancreatic cancer is associated with impaired glucose metabolism. *Eur J Surg* 1993; 159: 101-107 (PMID: 8098623)

8 Ogren M, Bergqvist D, Wåhlander K, Eriksson H, Sternby NH. Trousseau's syndrome - what is the evidence? A population-based autopsy study. *Thromb Haemost* 2006; 95541-545 (PMID: 16525584)

9 Cameron JL, Riall TS, Coleman J, Belcher KA. One thousand consecutive pancreaticoduodenectomies. *Ann Surg* 2006; 244: 10-15 (PMID: 16794383 DOI: 10.1097/01.sla.0000217673.04165. ea)

10 Levine WC, Mehta V, Landesberg G. Anesthesia for the el-derly: selected topics. *Curr Opin Anaesthesiol* 2006; 19: 320-324 (PMID: 16735817 DOI: 10.1097/01.aco.0000192807.63785.59)

11 Ackland GL, Edwards M. Defining higher-risk surgery. *Curr Opin Crit Care* 2010; 16: 339-346 (PMID: 20489608 DOI: 10.1097/MCC.0b013e328339fad5)

12 Kullavanijaya P, Treeprasertsuk S, Thong-Ngam D, Kladcha-roen N, Mahachai V, Suwanagool P. Adenocarcinoma of the pancreas: the clinical experience of 45 histopathologically proven patients, a 6 year study. *J Med Assoc Thai* 2001; 84: 640-647 (PMID: 11560212)

13 Dimick JB, Cowan JA, Upchurch GR, Colletti LM. Hospi-tal volume and surgical outcomes for elderly patients with colorectal cancer in the United States. *J Surg Res* 2003; 114:50-56 (PMID: 13678698 DOI: 10.1016/S0022-4804(03)00207-5)

14 La Torre M, Ziparo V, Nigri G, Cavallini M, Balducci G, Ramacciato G. Malnutrition and pancreatic surgery: preva-lence and outcomes. *J Surg Oncol* 2013; 107: 702-708 (PMID: 23280557 DOI: 10.1002/jso.23304)

15 Studley HO. Percentage of weight loss: a basic indicator of surgical risk in patients with chronic peptic ulcer. 1936. *Nutr Hosp* 2001; 16: 141-143; discussion 140-141 (PMID: 11680474)

16 Fleisher LA. Cardiac risk stratification for noncardiac sur-gery: update from the American College of Cardiology/ American Heart Association 2007 guidelines. *Cleve Clin J Med* 2009; 76 Suppl 4: S9-15 (PMID: 19880841 DOI: 10.3949/ ccjm.76.s4.02)

17 Hollingsworth KG, Blamire AM, Keavney BD, Macgowan GA. Left ventricular torsion, energetics, and diastolic func-tion in normal human aging. *Am J Physiol Heart Circ Physiol* 2012; 302: H885-H892 (PMID: 22180656 DOI: 10.1152/ajp-heart.00985.2011)

18 Nair D, Shlipak MG, Angeja B, Liu HH, Schiller NB, Whooley MA. Association of anemia with diastolic dysfunction among patients with coronary artery disease in the Heart and Soul Study. Am J Cardiol 2005; 95: 332-336 (PMID: 15670540 DOI: 10.1016/j.amjcard.2004.09.029)

19 Filipovic M, Wang J, Michaux I, Hunziker P, Skarvan K, Seeberger MD. Effects of halothane, sevoflurane and propo-fol on left ventricular diastolic function in humans during spontaneous and mechanical ventilation. Br J Anaesth 2005; 94: 186-192 (PMID: 15556965 DOI: 10.1093/bja/aei028)

20 Schmidt C, Hinder F, Van Aken H, Theilmeier G, Bruch C, Wirtz SP, Bürkle H, Gühs T, Rothenburger M, Berendes E. The effect of high thoracic epidural anesthesia on systolic and diastolic left ventricular function in patients with coro-nary artery disease. Anesth Analg 2005; 100: 1561-1569 (PMID: 15920175 DOI: 10.1213/01.ANE.0000154963.29271.36)

21 Alagiakrishnan K, Banach M, Jones LG, Datta S, Ahmed A, Aronow WS. Update on diastolic heart failure or heart failure with preserved ejection fraction in the older adults. Ann Med 2013; 45: 37-50 (PMID: 22413912 DOI: 10.3109/07853890.2012.660493)

22 Gullo L, Pezzilli R, Morselli-Labate AM. Diabetes and the risk of pancreatic cancer. *N Engl J Med* 1994; 331: 81-84 (PMID: 8208269 DOI: 10.1056/NEJM199407143310203)

4. 23 Permert J, Ihse I, Jorfeldt L, von Schenck H, Arnqvist HJ, Larsson J. Pancreatic cancer is associated with impaired glucose metabolism. *Eur J Surg* 1993; 159: 101-107 (PMID: 8098623)

24 Treiman GS, Treiman RL, Foran RF, Cossman DV, Cohen JL, Levin PM, Wagner WH, Davidson MB. The influence of diabetes mellitus on the risk of abdominal aortic surgery. *Am Surg* 1994; 60: 436-440 (PMID: 8198336)

25 Verhofstad MH, Hendriks T. Complete prevention of impaired anastomotic healing in diabetic rats requires preop-erative blood glucose control. *Br J Surg* 1996; 83: 1717-1721 (PMID: 9038550)

26 Zacharias A, Habib RH. Factors predisposing to median sternotomy complications. Deep vs superficial infection. *Chest* 1996; 110: 1173-1178 (PMID: 8915216)

27 Clement S, Braithwaite SS, Magee MF, Ahmann A, Smith EP, Schafer RG, Hirsch IB. Management of diabetes and hyperglycemia in hospitals. *Diabetes Care* 2004; 27: 553-591 (PMID: 14747243)

28 Coursin DB, Connery LE, Ketzler JT. Perioperative diabetic and hyperglycemic management issues. *Crit Care Med* 2004; 32: S116-S125 (PMID: 15064670)

29 Furnary AP, Gao G, Grunkemeier GL, Wu Y, Zerr KJ, Bookin SO, Floten HS, Starr A. Continuous insulin infusion reduces mortality in patients with diabetes undergoing cor-onary artery bypass grafting. *J Thorac Cardiovasc Surg* 2003; 125: 1007-1021 (PMID: 12771873 DOI: 10.1067/mtc.2003.181)

30 Goldberg PA, Siegel MD, Sherwin RS, Halickman JI, Lee M, Bailey VA, Lee SL, Dziura JD, Inzucchi SE. Implementation of a safe and effective insulin infusion protocol in a medical intensive care unit. *Diabetes Care* 2004; 27: 461-467 (PMID: 14747229)

31 Rehman HU, Mohammed K. Perioperative management of diabetic patients. *Curr Surg* 2003; 60: 607-611 (PMID: 14972202 DOI: 10.1016/j.cursur.2003.07.002)

32 Johnson RG, Arozullah AM, Neumayer L, Henderson WG, Hosokawa P, Khuri SF. Multivariable predictors of postop-erative respiratory failure after general and vascular surgery: results from the patient safety in surgery study. *J Am Coll Surg* 2007; 204: 1188-1198 (PMID: 17544077 DOI: 10.1016/ j.jamcollsurg.2007.02.070)

33 Khuri SF, Henderson WG, DePalma RG, Mosca C, Healey NA, Kumbhani DJ. Determinants of long-term survival after major surgery and the adverse effect of postoperative com-plications. *Ann Surg* 2005; 242: 326-341; discussion 341-343(PMID: 16135919)

34 Canet J, Gallart L, Gomar C, Paluzie G, Vallès J, Castillo J, Sabaté S, Mazo V, Briones Z, Sanchis J. Prediction of post-operative pulmonary complications in a population-based surgical cohort. *Anesthesiology* 2010; 113: 1338-1350 (PMID: 21045639 DOI: 10.1097/ALN.0b013e3181fc6e0a)

35 Canet J, Gallart L. Predicting postoperative pulmonary complications in the general population. *Curr Opin Anaes-thesiol* 2013; 26: 107-115 (PMID: 23407154 DOI: 10.1097/ACO.0b013e32835e8acd)

36 Lawrence VA, Dhanda R, Hilsenbeck SG, Page CP. Risk of pulmonary complications after elective abdominal surgery. *Chest* 1996; 110: 744-750 (PMID: 8797421)

37 Gass GD, Olsen GN. Preoperative pulmonary function test-ing to predict postoperative morbidity and mortality. *Chest* 1986; 89: 127-135 (PMID: 3940774)

38 Mourão F, Amado D, Ravasco P, Vidal PM, Camilo ME. Nutritional risk and status assessment in surgical patients: a challenge amidst plenty. *Nutr Hosp* 2004; 19: 83-88 (PMID: 15049409)

39 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40:373-383 (PMID: 3558716 DOI: 10.1016/0021-9681(87)90171-8)

40 Gibbs J, Cull W, Henderson W, Daley J, Hur K, Khuri SF. Preoperative serum albumin level as a predictor of opera-tive mortality and morbidity: results from the National VA Surgical Risk Study. *Arch Surg* 1999; 134: 36-42 (PMID: 9927128)

41 Koretz RL, Lipman TO, Klein S. AGA technical review on parenteral nutrition. *Gastroenterology* 2001; 121: 970-1001 (PMID: 11606512)

42 Jiang WG, Puntis MC. Immune dysfunction in patients with obstructive jaundice, mediators and implications for treat-ments. *HPB Surg* 1997; 10: 129-142 (PMID: 9174857)

43 Gould MK, Garcia DA, Wren SM, Karanicolas PJ, Arcelus JI,Heit JA, Samama CM. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; 141: e227S-e277S (PMID: 22315263)

44 Khorana AA, Fine RL. Pancreatic cancer and thromboem-bolic disease. *Lancet Oncol* 2004; 5: 655-663 (PMID: 15522652 DOI: 10.1016/S1470-2045(04)01606-7)

45 Caprini JA, Arcelus JI, Hasty JH, Tamhane AC, Fabrega F. Clinical assessment of venous thromboembolic risk in surgi-cal patients. *Semin Thromb Hemost* 1991; 17 Suppl 3: 304-312(PMID: 1754886)

46 Bozzato S, Galli L, Ageno W. Thromboprophylaxis in surgi-cal and medical patients. *Semin Respir Crit Care Med* 2012; 33:163-175 (PMID: 22648489 DOI: 10.1055/s-0032-1311795)

47 Bergqvist D, Agnelli G, Cohen AT, Eldor A, Nilsson PE, Le Moigne-Amrani A, Dietrich-Neto F. Duration of prophylaxis against venous thromboembolism with enoxaparin after surgery for cancer. *N Engl J Med* 2002; 346: 975-980 (PMID: 11919306 DOI: 10.1056/NEJMoa012385)

48 Douketis JD, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, Eckman MH, Dunn AS, Kunz R. Perioperative manage-ment of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guide-lines. *Chest* 2012; 141: e326S-e350S (PMID: 22315266)

49 Carli F, Kehlet H, Baldini G, Steel A, McRae K, Slinger P, Hemmerling T, Salinas F, Neal JM. Evidence basis for re-gional anesthesia in multidisciplinary fast-track surgical care pathways. *Reg Anesth Pain Med* 2011; 36: 63-72 (PMID: 22002193 DOI: 10.1097/AAP.0b013e31820307f7)

50 Clemente A, Carli F. The physiological effects of thoracic epidural anesthesia and analgesia on the cardiovascular, respiratory and gastrointestinal systems. *Minerva Anestesiol* 2008; 74: 549-563 (PMID: 18854796)

51 Treschan TA, Taguchi A, Ali SZ, Sharma N, Kabon B, Sessler DI, Kurz A. The effects of epidural and general anesthesia on tissue oxygenation. Anesth ANALG2003;96 1553-1557(PMID:12760974 DOI:10.1213/01.ANE.0000063824.43113.DB)

52 Kabon B, Fleischmann E, Treschan T, Taguchi A, Kapral S, Kurz A. Thoracic epidural anesthesia increases tis-sue oxygenation during major abdominal surgery. *Anesth Analg* 2003; 97: 1812-1817 (PMID: 14633566 DOI: 10.1213/01. ANE.0000087040.48267.54)

53 Moraca RJ, Sheldon DG, Thirlby RC. The role of epidu-ral anesthesia and analgesia in surgical practice. *Ann Surg* 2003; 238: 663-673 (PMID: 14578727 DOI: 10.1097/01. sla.0000094300.36689.ad)

54 Snyder GL, Greenberg S. Effect of anaesthetic technique and other perioperative factors on cancer recurrence. *Br J An-aesth* 2010; 105: 106-115 (PMID: 20627881 DOI: 10.1093/bja/ aeq164)

55 Gottschalk A, Ford JG, Regelin CC, You J, Mascha EJ, Sessler DI, Durieux ME, Nemergut EC. Association between epidu-ral analgesia and cancer recurrence after colorectal cancer surgery. *Anesthesiology* 2010; 113: 27-34 (PMID: 20508494 DOI: 10.1097/ALN.0b013e3181de6d0d)

56 National Nosocomial Infections Surveillance (NNIS) report, data summary from October 1986-April 1996, issued May 1996. A report from the National Nosocomial Infections Sur-veillance (NNIS) System. *Am J Infect Control* 1996; 24: 380-388 (PMID: 8902113 DOI: 10.1016/S0196-6553(96)90026-7)

57 Mauermann WJ, Nemergut EC. The anesthesiologist's role in the prevention of surgical site infections. *Anest-*

hesiology 2006; 105: 413-421; quiz 439-440 (PMID: 16871076 DOI: 10.10 97/00000542-200608000-00025)

58 Anderson DJ, Kaye KS, Classen D, Arias KM, Podgorny K, Burstin H, Calfee DP, Coffin SE, Dubberke ER, Fraser V, Gerding DN, Griffin FA, Gross P, Klompas M, Lo E, Marschall J, Mermel LA, Nicolle L, Pegues DA, Perl TM, Saint S, Salgado CD, Weinstein RA, Wise R, Yokoe DS. Strat-egies to prevent surgical site infections in acute care hospi-tals. *Infect Control Hosp Epidemiol* 2008; 29 Suppl 1: S51-S61 (PMID: 18840089 DOI: 10.1086/591064)

59 Haynes AB, Weiser TG, Berry WR, Lipsitz SR, Breizat AH, Dellinger EP, Herbosa T, Joseph S, Kibatala PL, Lapitan MC, Merry AF, Moorthy K, Reznick RK, Taylor B, Gawande AA. A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med* 2009; 360: 491-499 (PMID: 19144931 DOI: 10.1056/NEJMsa0810119)

60 de Vries EN, Prins HA, Crolla RM, den Outer AJ, van Andel G, van Helden SH, Schlack WS, van Putten MA, Gouma DJ, Dijkgraaf MG, Smorenburg SM, Boermeester MA. Effect of a comprehensive surgical safety system on patient outcomes. *N Engl J Med* 2010; 363: 1928-1937 (PMID: 21067384 DOI: 10.1056/NEJMsa0911535)

61 Polk HC, Lopez-Mayor JF. Postoperative wound infection: a prospective study of determinant factors and prevention. *Surgery* 1969; 66: 97-103 (PMID: 4892316)

62 Diana M, Hübner M, Eisenring MC, Zanetti G, Troillet N, Demartines N. Measures to prevent surgical site infections: what surgeons (should) do. *World J Surg* 2011; 35: 280-288 (PMID: 21088838 DOI: 10.1007/s00268-010-0862-0)

63 Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hos-pital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 1999; 20: 250-278; quiz 279-280 (PMID: 10219875 DOI: 10.1086/501620)

64 ASHP Therapeutic Guidelines on Antimicrobial Prophylaxis in Surgery. American Society of Health-System Pharmacists. *Am J Health Syst Pharm* 1999; 56: 1839-1888 (PMID: 10511234)

65 Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Tem-perature Group. *N Engl J Med* 1996; 334: 1209-1215 (PMID: 8606715 DOI: 10.1056/NEJM199605093341901)

66 Sesler DI. Complications and treatment of mild hypother MİA. Anesthesiology 2001 ;95:531-543 (PMID:11506130 DOI:10.1097/00000542-200108000-00040)

67 Sessler DI, Akça O. Nonpharmacological prevention of surgical wound infections. *Clin Infect Dis* 2002; 35: 1397-140(PMID: 12439804 DOI: 10.1086/344275)

68 Hopf HW, Hunt TK, West JM, Blomquist P, Goodson WH, Jensen JA, Jonsson K, Paty PB, Rabkin JM, Upton RA, von Smitten K, Whitney JD. Wound tissue oxygen tension pre-dicts the risk of wound infection in surgical patients. *Arch Surg* 1997; 132: 997-1004; discussion 1005 (PMID: 9301613 DOI: 10.1001/archsurg.1997.01430330063010)

69 Bräuer A, Quintel M. Forced-air warming: technology, physical background and practical aspects. *Curr Opin An-aesthesiol* 2009; 22: 769-774 (PMID: 19734783 DOI: 10.1097/ACO.0b013e328331d134)

70 Bräuer A, Bovenschulte H, Perl T, Zink W, English MJ Quintel M. What determines the efficacy of forced-air warm-ing systems? A manikin evaluation with upper body blan-kets. *Anesth Analg* 2009; 108: 192-198 (PMID: 19095849 DOI:10.1213/ane.0b013e31818e0cee)

71 Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hy-perglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. *Lancet* 2000; 355: 773-778 (PMID: 10711923 DOI:10.1016/S0140-6736(99)08415-9)

72 Cheadle WG. Risk factors for surgical site infection. *Surg In-fect* (Larchmt) 2006; 7 Suppl 1: S7-S11 (PMID: 16834549 DOI:10.1089/sur.2006.7.s1-7)

73 van den Berghe G, Wouters P, Weekers F, Verwaest C,Bruyninckx F, Schetz M, Vlasselaers D, Ferdinande P, Lauw-ers P, Bouillon R. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001; 345: 1359-1367 (PMID: 11794168 DOI: 10.1056/NEJMoa011300)

74 Kersten JR, Warltier DC, Pagel PS. Aggressive control of intraoperative blood glucose concentration: a shifting para-digm? *Anesthesiology* 2005; 103: 677-678 (PMID: 16192757 DOI: 10.1097/00000542-200510000-00002)

75 Tartter PI, Quintero S, Barron DM. Perioperative blood transfusion associated with infectious complications after colorectal cancer operations. *Am J Surg* 1986; 152: 479-482 (PMID: 3777324 DOI: 10.1016/0002-9610(86)90207-2)

76 Raghavan M, Marik PE. Anemia, allogenic blood transfu-sion, and immunomodulation in the critically ill. *Chest* 2005; 127: 295-307 (PMID: 15653997 DOI: 10.1378/chest.127.1.295)

77 Carson JL, Noveck H, Berlin JA, Gould SA. Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion. *Transfusion* 2002; 42: 812-818 (PMID: 12375651 DOI: 10.1046/j.1537-2995.2002.00123.x)

78 Carson JL, Duff A, Poses RM, Berlin JA, Spence RK, Trout R, Noveck H, Strom BL. Effect of anaemia and cardio-vascular disease on surgical mortality and morbidity. *Lancet* 1996; 348: 1055-1060 (PMID: 8874456 DOI: 10.1016/ S0140-6736(96)04330-9)

79 Hébert PC, Yetisir E, Martin C, Blajchman MA, Wells G, Marshall J, Tweeddale M, Pagliarello G, Schweitzer I. Is a low transfusion threshold safe in

critically ill patients with cardiovascular diseases? Crit Care Med 2001;29:227-234 (PMID:11246298 DOI:1097/00003246-200202000-00001)

5. 80 Goodnough LT, Levy JH, Murphy MF. Concepts of blood transfusion in adults. *Lancet* 2013; 381: 1845-1854 (PMID: 23706801 DOI: 10.1016/S0140-6736(13)60650-9)

81 Shander A, Fink A, Javidroozi M, Erhard J, Farmer SL, Corwin H, Goodnough LT, Hofmann A, Isbister J, Ozawa

6. S, Spahn DR. Appropriateness of allogeneic red blood cell transfusion: the international consensus conference on trans-fusion outcomes. *Transfus Med Rev* 2011; 25: 232-246.e5(PMID: 21498040)

82 American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American So-ciety of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. *Anesthesiology* 2006; 105: 198-208 (PMID: 16810012 DOI: 10.1097/00000542-200607000-00030)

83 Carson JL, Grossman BJ, Kleinman S, Tinmouth AT, Marques MB, Fung MK, Holcomb JB, Illoh O, Kaplan LJ,Katz LM, Rao SV, Roback JD, Shander A, Tobian AA, Wein-stein R, Swinton McLaughlin LG, Djulbegovic B. Red blood cell transfusion: a clinical practice guideline from the AABB*. *Ann Intern Med* 2012; 157: 49-58 (PMID: 22751760 DOI: 10.7326/0003-4819-157-1-201206190-00429)

84 10O Kozek-Langenecker SA, Afshari A, Albaladejo P, San-tullano CA, De Robertis E, Filipescu DC, Fries D, Görlinger K, Haas T, Imberger G, Jacob M, Lancé M, Llau J, Mallett S, Meier J, Rahe-Meyer N, Samama CM, Smith A, Solomon C, Van der Linden P, Wikkelsø AJ, Wouters P, Wyffels P. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. *Eur J An-aesthesiol* 2013; 30: 270-382 (PMID: 23656742 DOI: 10.1097/EJA.0b013e32835f4d5b)

85 Chappell D, Jacob M, Hofmann-Kiefer K, Conzen P, RehmM. A rational approach to perioperative fluid management. *Anesthesiology* 2008; 109: 723-740 (PMID: 18813052 DOI:10.1097/ALN.0b013e3181863117)

86 Futier E, Constantin JM, Petit A, Chanques G, Kwiatkowski F, Flamein R, Slim K, Sapin V, Jaber S, Bazin JE. Conservative vs restrictive individualized goal-directed fluid replacement strategy in major abdominal surgery: A prospective random-ized trial. *Arch Surg* 2010; 145: 1193-1200 (PMID: 21173294 DOI: 10.1001/archsurg.2010.275)

87 Jacob M, Chappell D, Rehm M. Clinical update: perioperative fluid management. *Lancet* 2007; 369: 1984-1986 (PMID:17574081 DOI: 10.1016/S0140-6736(07)60926-X)

88 Lobo DN, Bostock KA, Neal KR, Perkins AC, Rowlands BJ, Allison SP. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. *Lancet* 2002; 359: 1812-1818(PMID: 12044376 DOI: 10.1016/S0140-6736(02)08711-1)

89 Holte K, Sharrock NE, Kehlet H. Pathophysiology and clini-cal implications of perioperative fluid excess. *Br J Anaesth* 2002; 89: 622-632 (PMID: 12393365 DOI: 10.1093/bja/aef220)

90 Gurgel ST, do Nascimento P. Maintaining tissue perfu-sion in high-risk surgical patients: a systematic review of randomized clinical trials. *Anesth Analg* 2011; 112: 1384-1391(PMID: 21156979 DOI: 10.1213/ANE.0b013e3182055384)

7. 91 Baron JF, De Kegel D, Prost AC, Mundler O, Arthaud M, Basset G, Maistre G, Masson F, Carayon A, Landault C. Low molecular weight hydroxyethyl starch 6% compared to albu-min 4% during intentional hemodilution. *Intensive Care Med* 1991; 17: 141-148 (PMID: 1712801 DOI: 10.1007/BF01704717)

8. 92 Nisanevich V, Felsenstein I, Almogy G, Weissman C, Einav S,Matot I. Effect of intraoperative fluid management on outcome after intraabdominal surgery. *Anesthesiology* 2005; 103: 25-32(PMID: 15983453 DOI: 10.1097/00000542-200507000-00008)

93 Joshi GP. Intraoperative fluid restriction improves out-come after major elective gastrointestinal surgery. Anesth Analg 2005;101: 601-605 (PMID:16037184 DOI:10.1213/01.ANE.0000159171.26521.31)

94 Kimberger O, Arnberger M, Brandt S, Plock J, Sigurdsson GH, Kurz A, Hiltebrand L. Goal-directed colloid administra-tion improves the microcirculation of healthy and perian-astomotic colon. *Anesthesiology* 2009; 110: 496-504 (PMID: 19225390 DOI: 10.1097/ALN.0b013e31819841f6)

95 Hamilton MA, Cecconi M, Rhodes A. A systematic re-view and meta-analysis on the use of preemptive hemo-dynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. *Anesth Analg* 2011; 112: 1392-1402 (PMID: 20966436 DOI: 10.1213/ANE.0b013e3181eeaae5)

96 Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the lit-erature and the tale of seven mares. *Chest* 2008; 134: 172-178(PMID: 18628220 DOI: 10.1378/chest.07-2331)

97 Peng ZY, Kellum JA. Perioperative fluids: a clear road ahead? *Curr Opin Crit Care* 2013; 19: 353-358 (PMID: 23817030 DOI: 10.1097/MCC.0b013e3283632f1f)

98 Wakeling HG, McFall MR, Jenkins CS, Woods WG, Miles WF, Barclay GR, Fleming SC. Intraoperative oesophageal Doppler guided fluid management shortens postoperative hospital stay after major bowel surgery. *Br J Anaesth* 2005; 95:634-642 (PMID: 16155038 DOI: 10.1093/bja/aei223)

99 Bundgaard-Nielsen M, Holte K, Secher NH, Kehlet H. Moni-toring of peri-operative fluid administration by individual-ized goal-directed therapy. *Acta Anaesthesiol Scand* 2007; 51: 331-340 (PMID: 17390421 DOI: 10.1111/j.1399-6576.2006.01221. x)

100 Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsive-ness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med* 2009; 37: 2642-2647 (PMID: 19602972 DOI: 10.1097/CCM.0b013e3181a590da)

101 Chappell D, Westphal M, Jacob M. The impact of the gly-cocalyx on microcirculatory oxygen distribution in critical illness. *Curr Opin Anaesthesiol* 2009; 22: 155-162 (PMID: 19307890 DOI: 10.1097/ACO.0b013e328328d1b6)

102 De Backer D, Donadello K, Taccone FS, Ospina-Tascon G, Salgado D, Vincent JL. Microcirculatory alterations: potential mechanisms and implications for therapy. *Ann Intensive Care* 2011; 1: 27 (PMID: 21906380 DOI: 10.1186/2110-5820-1-27)

103 Perner A, Haase N, Guttormsen AB, Tenhunen J, Klemen-zson G, Åneman A, Madsen KR, Møller MH, Elkjær JM, Poulsen LM, Bendtsen A, Winding R, Steensen M, Berezo-wicz P, Søe-Jensen P, Bestle M, Strand K, Wiis J, White JO, Thornberg KJ, Quist L, Nielsen J, Andersen LH, Holst LB, Thormar K, Kjældgaard AL, Fabritius ML, Mondrup F, Pott FC, Møller TP, Winkel P, Wetterslev J. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. *N Engl J Med* 2012; 367: 124-134 (PMID: 22738085 DOI: 10.1056/NEJ-Moa1204242)

104 Myburgh JA, Finfer S, Bellomo R, Billot L, Cass A, Gattas D, Glass P, Lipman J, Liu B, McArthur C, McGuinness S, Rajbhandari D, Taylor CB, Webb SA. Hydroxyethyl starch or saline for resuscitioon in intensive care.N Engl J Med 0212; 367:1901-1911 (PMID: 23075127 DOI:10. 1056/NEJ-M oa1209759)

105 Lobo SM, Mendes CL, Rezende E, Dias FS. Optimizing perioperative hemodynamics: what is new? *Curr Opin Crit Care* 2013; 19: 346-352 (PMID: 23817029 DOI: 10.1097/MCC.0b013e3283632ef1)

106 Holte K, Foss NB, Svensén C, Lund C, Madsen JL, Kehlet H. Epidural anesthesia, hypotension, and changes in intra-vascular volume. *Anesthesiology* 2004; 100: 281-286 (PMID: 14739801 DOI: 10.1097/00000542-200402000-00016)

107 Hedenstierna G, Edmark L. The effects of anesthesia and muscle paralysis on the respiratory system. *Intensive Care Med* 2005; 31: 1327-1335 (PMID: 16132894 DOI: 10.1007/ s00134-005-2761-7)

108 Reinius H, Jonsson L, Gustafsson S, Sundbom M, Duvernoy O, Pelosi P, Hedenstierna G, Fredén F. Prevention of atelec-tasis in morbidly obese patients during general anesthesia and paralysis: a computerized tomography study. *Anesthe-siology* 2009; 111: 979-987 (PMID: 19809292 DOI: 10.1097/ALN.0b013e3181b87edb)

109 Sundar S, Novack V, Jervis K, Bender SP, Lerner A, Panzica P, Mahmood F, Malhotra A, Talmor D. Influence of low tidal volume ventilation on time to extubation in cardiac surgical patients. *Anesthesiology* 2011; 114: 1102-1110 (PMID: 21430518 DOI: 10.1097/ALN.0b013e318215e254)

110 Talab HF, Zabani IA, Abdelrahman HS, Bukhari WL, Ma-moun I, Ashour MA, Sadeq BB, El Sayed SI. Intraoperative ventilatory strategies for prevention of pulmonary atelectasis in obese patients undergoing laparoscopic bariatric surgery. *Anesth Analg* 2009; 109: 1511-1516 (PMID: 19843790 DOI: 10.1213/ANE.0b013e3181ba7945)

111 Severgnini P, Selmo G, Lanza C, Chiesa A, Frigerio A, Bacuzzi A, Dionigi G, Novario R, Gregoretti C, de Abreu MG, Schultz MJ, Jaber S, Futier E, Chiaranda M, Pelosi P. Protective mechanical ventilation during general anesthesia for open abdominal surgery improves postoperative pul-monary function. *Anesthesiology* 2013; 118: 1307-1321 (PMID: 23542800 DOI: 10.1097/ALN.0b013e31829102de)

112 McCrath DJ, Cerboni E, Frumento RJ, Hirsh AL, Bennett-Guerrero E. Thromboelastography maximum amplitude predicts postoperative thrombotic complications including myocardial infarction. *Anesth Analg* 2005; 100: 1576-1583 (PMID: 15920177 DOI: 10.1213/01.ANE.0000155290.86795.12)

113 Kashuk JL, Moore EE, Sabel A, Barnett C, Haenel J, Le T, Pezold M, Lawrence J, Biffl WL, Cothren CC, Johnson JL. Rapid thrombelastography (r-TEG) identifies hypercoagu-lability and predicts thromboembolic events in surgical pa-tients. *Surgery* 2009; 146: 764-772; discussion 772-774 (PMID: 19789037)

114 Kehlet H. Labat lecture 2005: surgical stress and postopera-tive outcome-from here to where? *Reg Anesth Pain Med* 2005; 31: 47-52 (PMID: 16418025)

115 Ypsilantis E, Praseedom RK. Current status of fast-track re-covery pathways in pancreatic surgery. *JOP* 2009; 10: 646-650(PMID: 19890186)

116 Fuks D, Piessen G, Huet E, Tavernier M, Zerbib P, Michot F, Scotte M, Triboulet JP, Mariette C, Chiche L, Salame E, Segol P, Pruvot FR, Mauvais F, Roman H, Verhaeghe P, Regim-beau JM. Life-threatening postoperative pancreatic fistula (grade C) after pancreaticoduodenectomy: incidence, prog-nosis, and risk factors. *Am J Surg* 2009; 197: 702-709 (PMID: 18778804 DOI: 10.1016/j.amjsurg.2008.03.004

117 Diks J, van Hoorn DE, Nijveldt RJ, Boelens PG, Hofman Z, Bouritius H, van Norren K, van Leeuwen PA. Preoperative fasting: an outdated concept? *JPEN J Parenter Enteral Nutr* 2005; 29: 298-304 (PMID: 15961687 DOI: 10.1177/0148607105 029004298

118 Moore FA, Feliciano DV, Andrassy RJ, McArdle AH, Booth FV, Morgenstein-Wagner TB, Kellum JM, Welling RE, Moore Early enteral feeding, compared with parenteral, reduces postoperative septic complications. The results of a meta-analysis. *Ann Surg* 1992; 216: 172-183 (PMID: 1386982 DOI:10.1097/00000658-199208000-00008)

119 Slezak LA, Andersen DK. Pancreatic resection: effects on glucose metabolism. *World J Surg* 2001; 25: 452-460 (PMID: 11344398 DOI: 10.1007/s002680020337)

120 Nosadini R, del Prato S, Tiengo A, Duner E, Toffolo G, Cobelli C, Faronato PP, Moghetti P, Muggeo M.

Insulin sensitivity, binding, and kinetics in pancreatogenic and type 1diabetes. *Diabetes* 1982; 31: 346-355 (PMID: 6759250 DOI: 10.2337/diab.31.4.346)

121 Duron F, Duron JJ. Pancreatectomy and diabetes. *Ann Chir* 1999; 53: 406-411 (PMID: 10389330)

122 Dresler CM, Fortner JG, McDermott K, Bajorunas DR. Meta-bolic consequences of (regional) total pancreatectomy. *Ann Surg* 1991; 214: 131-140 (PMID: 1867520 DOI: 10.1097/00000658-199108000-00007

123 Van den Berghe G. Insulin therapy in the intensive care unit should be targeted to maintain blood glucose between 4.4 mmol/l and 6.1 mmol/l. *Diabetologia* 2008; 51: 911-915 (PMID: 18040662 DOI: 10.1007/s00125-007-0878-7)

124 Ballantyne JC, Carr DB, deFerranti S, Suarez T, Lau J, Chalmers TC, Angelillo IF, Mosteller F. The comparative ef-fects of postoperative analgesic therapies o pulmonary out-come: cumulative meta-analyses of randomized, controlled trials. *Anesth Analg* 1998; 86: 598-612 (PMID: 9495424)

125 Holte K, Kehlet H. Effect of postoperative epidural analgesia on surgical outcome. *Minerva Anestesiol* 2002; 68: 157-161 (PMID: 12024074)

126 Uchida I, Asoh T, Shirasaka C, Tsuji H. Effect of epidural analgesia on postoperative insulin resistance as evaluated by insulin clamp technique. *Br J Surg* 1988; 75: 557-562 (PMID: 3293693 DOI: 10.1002/bjs.1800750618)

127 Rodgers A, Walker N, Schug S, McKee A, Kehlet H, van Zundert A, Sage D, Futter M, Saville G, Clark T, MacMahon S. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of ran-domised trials. *BMJ* 2000; 321: 1493 (PMID: 11118174 DOI: 10.1136/bmj.321.7275.1493)

128 Steinbrook RA. Epidural anesthesia and gastrointestinal motility. *Anesth Analg* 1998; 86: 837-844 (PMID: 9539611)

129 Liu SS, Carpenter RL, Mackey DC, Thirlby RC, Rupp SM, Shine TS, Feinglass NG, Metzger PP, Fulmer JT, Smith SL. Effects of perioperative analgesic technique on rate of re-covery after colon surgery. *Anesthesiology* 1995; 83: 757-765 (PMID:757455 DOI: 10.1097/00000542-199510000-00015)

130 Haines KJ, Skinner EH, Berney S. Association of postopera-tive pulmonary complications with delayed mobilisation following major abdominal surgery: an observational cohort study. *Physiotherapy* 2013; 99: 119-125 (PMID: 23219632)

131 Manzano RM, Carvalho CR, Saraiva-Romanholo BM, Vieira JE. Chest physiotherapy during immediate postoperative pe-riod among patients undergoing upper abdominal surgery: randomized clinical trial. *Sao Paulo Med J* 2008; 126: 269-273 (PMID: 19099160 DOI: 10.1590/S1516-31802008000500005)

132 Chawla G, Drummond GB. Fentanyl decreases end-expi-ratory lung volume in patients anaesthetized with sevoflu-rane. *Br J Anaesth* 2008; 100: 411-414 (PMID: 18216033 DOI: 10.1093/bja/aem376)

133 Warner DO. Preventing postoperative pulmonary complica-tions: the role of the anesthesiologist. *Anesthesiology* 2000; 92:1467-1472 (PMID: 10781293 DOI: 10.1097/00000542-200005000-00037)

134 Witkowski ER, Smith JK, Tseng JF. Outcomes following resection of pancreatic cancer. *J Surg Oncol* 2013; 107: 97-103 (PMID: 22991309 DOI: 10.1002/jso.23267)