(1) Question 4

Answer B: Her duration of RRT will be shorter

Educational objective: Cite the impact of angiotensin II on patients with shock and acute kidney injury In the Angiotensin II for the Treatment of High-Output Shock 3 (ATHOS-3) trial, patients with vasodilatory shock received angiotensin II or placebo. The primary endpoint was an increase in the mean arterial pressure (MAP) of at least 10 mmHg or an increase the MAP to at least 75 mmHg within 3 hours of drug administration. Thus, an increase from 65 to 75 as noted in this patient would have met the primary endpoint of this trial. Patients with acute kidney injury on renal replacement therapy (RRT) receiving angiotensin II were more likely to be alive and off RRT in seven days compared to those receiving placebo. Hence, option B is correct. While angiotensin II did improve the chances of meeting this endpoint, there was no significant difference in inpatient mortality. Therefore, option A is incorrect. The increase in MAP from angiotensin II was associated with a decrease in Sequential Organ Failure Assessment (SOFA) score (thus, option C is incorrect). No difference in duration of mechanical ventilation was observed (option D is incorrect).

• Khanna A, English SW, Wang XS, Ham K, Tumlin J, Szerlip HM, Busse LW, Altaweel L, Albertson TE, Mackey C, McCurdy MT, Boldt DW, Chock S, Young PJ, Krell K, Wunderink RG, Ostermann M, Murugan R, Gong MN, Panwar R, Hastbacka J, Favory R, Venkatesh B, Thompson BT, Bellomo R, Jensen J, Kroll S, Chawla LS, Tidmarsh GF, Deane AM: Angiotensin II for the treatment of vasodilatory shock. N Engl J Med 377: 419-430, 2017

• Tumlin JA, Murugan R, Deane AM, Ostermann M, Busse LW, Ham KR, Kashani K, Szerlip HM, Prowle JR, Bihorac A, Finkel KW, Zarbock A, Forni LG, Lynch SJ, Jensen J, Kroll S, Chawla LS,

• Tidmarsh GF, Bellomo R: Outcomes in patients with vasodilatory shock and renal replacement therapy treated with intravenous angiotensin II. Crit Care Med 2018

(2) Question 5

Answer B: An increased risk of AKI requiring RRT

Educational objective: Recognize the outcomes associated with a restrictive versus a liberal fluid strategy in the post-operative setting The REstrictive versus LIbEral Fluid therapy in major abdominal surgery (RELIEF) trial randomly assigned 3000 patients deemed to have an increased risk for post-operative complications to a fluid-liberal or a fluid-restrictive regimen for the first 24 hours after surgery. The fluid-liberal strategy included the use of balanced solutions at a dose of 10 ml/kg per h during anesthesia, 8 ml/kg per h during the surgical procedure, and then 1.5 ml/kg per h for the first 24 post-operative hours. The restrictive regimen was designed to provide net even fluid balance. An increased risk of acute kidney injury, more specifically, acute kidney injury requiring renal replacement therapy, was observed in the restrictive fluid group. Hence, option B is correct. Those in the restrictive arm were more likely to experience surgical site infections. Therefore, option A is incorrect. There was no difference in the length of ICU stay or one-year mortality (options C and D are incorrect).

• Myles PS, Bellomo R, Corcoran T, Forbes A, Peyton P, Story D, Christophi C, Leslie K, McGuinness S, Parke R, Serpell J, Chan MTV, Painter T, McCluskey S, Minto G, Wallace S: Restrictive versus liberal fluid therapy for major abdominal surgery. N Engl J Med 378: 2263-2274, 2018

(3) Question 6

Answer C: Decreased risk of progressive AKI requiring dialysis

Educational objective: Know the benefits and potential complications of 4.2% bicarbonate based solutions in the setting of advanced severe acute kidney injury, acidosis, and shock

Jaber and colleagues recently published a multi-center, open-label randomized controlled trial in which 389 ICU patients with a pH less than 7.20, PaCO2 ≤45 mmHg, and serum bicarbonate ≤20 mmol/L received either no bicarbonate or 4.2% sodium bicarbonate. The bicarbonate infusion was titrated to increase the arterial pH to 7.30. In the subset analysis of those with severe AKI (stage 2 or 3, like the patient described in this question), subjects treated with 4.2% sodium bicarbonate had a decreased rate of acute kidney injury requiring renal replacement therapy. Therefore, option C is correct. Patients with acute kidney injury receiving 4.2% sodium bicarbonate were found to have improved mortality at 28 days (option A is incorrect). While bicarbonate therapy was associated with a lower rate of hyperkalemia, it led to a higher incidence of metabolic alkalosis, hypernatremia, and hypocalcemia (not hypercalcemia; option B is incorrect). There was no significant impact of bicarbonate administration on the rate of ICU-delirium (option D is incorrect). Finally, bicarbonate usage was associated with more vasopressor-free days compared to those receiving no bicarbonate (option E is incorrect). There was no difference in ICU length of stay.

• Jaber S, Paugam C, Futier E, Lefrant JY, Lasocki S, Lescot T, Pottecher J, Demoule A, Ferrandiere M, Asehnoune K, Dellamonica J, Velly L, Abback PS, de Jong A, Brunot V, Belafia F, Roquilly A, Chanques G, Muller L, Constantin JM, Bertet H, Klouche K, Molinari N, Jung B: Sodium bicarbonate therapy for patients with severe metabolic acidaemia in the intensive care unit (BICAR-ICU): a multicentre, open-label, randomised controlled, phase 3 trial. Lancet 392: 31-40, 2018

(4) Question 11

Answer B: A decreased rate of stage 2 and 3 AKI

Educational objective: Understand the utility of TIMP2*IGFBP7 measurment in patients at risk for post-operative acute kidney injury

Two studies that have recently analyzed the impact of the Kidney Disease - Improving Global Outcomes (KDIGO) care bundles for patients with elevated post-operative urinary levels of TIMP2*IGFBP7. Both have shown a reduction in the rates of stage 2 and 3 acute kidney injury. Hence, option B is correct. Neither the study by Gocze et al. or Meersch et al. demonstrated a shorter length of mechanical ventialtion. Therefore, option A is incorrect. While the Prevention of cardiac surgery associated-AKI (PREV) group demonstrated a reduction in renal replacement therapy (RRT)-requiring AKI, the study by Gocze and colleagues failed to replicate this, although RRT rates were low in this non-cardiac surgery population. Thus, option C is not the best answer. Neither study demonstrated a mortality benefit (option D is incorrect) and both studies demonstrated an increase in urine output in the early post-operative period; thus option E is incorrect

• Meersch M, Schmidt C, Hoffmeier A, Van Aken H, Wempe C, Gerss J, Zarbock A: Prevention of cardiac surgery-associated AKI by implementing the KDIGO guidelines in high risk patients identified by biomarkers: the PrevAKI randomized controlled trial. Intensive Care Med 2017

• Gocze I, Jauch D, Gotz M, Kennedy P, Jung B, Zeman F, Gnewuch C, Graf BM, Gnann W, Banas B, Bein T, Schlitt HJ, Bergler T: Biomarker-guided Intervention to Prevent Acute Kidney Injury After Major Surgery: The Prospective Randomized BigpAK Study. Annals of surgery 2017

(5) Question 16

Answer C: Neither N-acetylcysteine compared to placebo nor isotonic bicarbonate therapy compared to saline is more likely to reduce the risk of dialysis-requiring AKI after contrast exposure

Educational objective: Cite recent evidence regarding the impact of prophylactic measures in the prevention of contrast-induced nephropathy in high risk patients

The Prevention of Serious Adverse Events Following Angiography (PRESERVE) trial examined high-risk patients undergoing cardiac angiography, including those with an eGFR between 30 and 59 ml/min per 1.73 m2 with either diabetes mellitus or an eGFR of <30 ml/min per 1.73 m2. N-acetylcysteine compared to placebo or isotonic bicarbonate compared to saline did not reduce the risk of AKI-requiring dialysis, death, or persistent worsening of renal function. Hence, option C is correct. The other listed options are not supported by PRESERVE and are incorrect.

• Weisbord SD, Gallagher M, Jneid H, Garcia S, Cass A, Thwin SS, Conner TA, Chertow GM, Bhatt DL, Shunk K, Parikh CR, McFalls EO, Brophy M, Ferguson R, Wu H, Androsenko M, Myles J, Kaufman J, Palevsky PM; PRESERVE Trial Group: Outcomes after angiography with sodium bicarbonate and acetylcysteine. N Engl J Med 378: 603-614, 2018

(6) Question 18

Answer B: It increases his risk of incident congestive heart failure

Educational objective: Know that acute kidney injury is associated with an increased risk of incident heart failure

In a large study of United States Veterans who were hospitalized and did not have a prior history of congestive heart failure, acute kidney injury (AKI) was associated with an increased risk incident congestive heart failure. Thus, option B is correct and option A is incorrect. This risk was not restricted to dialysis-requiring AKI (option C is incorrect) and was not dependent on recovery status (option D is incorrect).

• Bansal N, Matheny ME, Greevy RA Jr, Eden SK, Perkins AM, Parr SK, Fly J, Abdel-Kader K, Himmelfarb J, Hung AM, Speroff T, Ikizler TA, Siew ED: Acute Kidney Injury and Risk of Incident Heart Failure Among US Veterans. Am J Kidney Dis 71: 236-245, 2018

(7) Question 21

Answer D: Vancomycin nephrotoxicity has been associated with trough levels ?15 mg/L

Educational objective: Know that vancomycin trough level ?15 mg/L are associated with an increased risk of nephrotoxicity A recent meta-analysis examined the association between acute kidney injury and serum vancomycin levels. Of the initial 240 studies identified, 38 were reviewed, and 15 studies met the inclusion criteria. Overall, higher troughs (≥15 mg/L) were associated with 2.67-fold

increased odds of nephrotoxicity relative to trough levels <15 mg/L. Therefore, option D is correct and option A is incorrect. Vancomycin peak and trough levels are associated with nephrotoxicity. Hence, option B is incorrect. The absence of oliguria does not negate the need to adjust vancomycin dosing when there is a decline in kidney function. Thus, option C is incorrect.

• van Hal, SJ, Paterson, DL, Lodise, TP: Systematic review and meta-analysis of vancomycin-induced nephrotoxicity associated with dosing schedules that maintain troughs between 15 and 20 milligrams per liter. Antimicrob Agents Chemother, 57: 734-744, 2013

(8) Question 25

Answer D: Her pre-ESRD episode of AKI is associated with a 30% greater risk of mortality at 1 year in comparison with patients without AKI before incident dialysis

Educational objective: Identify acute kidney injury within two years of dialysis initiation as a risk factor for mortality Lee et al. evaluated the impact of prior episodes of acute kidney in a retrospective cohort of 47,341 incident hemodialysis patients from the United States Renal Data System with linked Medicare data for at least 2 years prior to hemodialysis initiation. The authors examined the relationship between AKI events in the 2-year pre-ESRD period on the type of vascular access used at hemodialysis initiation and 1-year all-cause mortality. AKI was associated with 1.3-fold greater odds of 1-year mortality after dialysis initiation. Hence, option D is correct and option A is incorrect. The authors also confirmed that this association was independent of type of dialysis vascular access used at the time of initial dialysis treatment (option B is incorrect). There is no compelling reason to initiate dialysis in the inpatient setting. Therefore, option C is incorrect.

• Lee T, Shah S, Leonard AC, Parikh P, Thakar CV: Acute Kidney Injury before Dialysis Initiation Predicts Adverse Outcomes in Hemodialysis Patients. Am J Nephrol 47: 427-434, 2018

• Wald R, Quinn RR, Luo J, Li P, Scales DC, Mamdani MM, Ray JG; University of Toronto Acute Kidney Injury Research Group: Chronic dialysis and death among survivors of acute kidney injury requiring dialysis. JAMA 302: 1179-1185, 2009

• Wald R, Quinn RR, Adhikari NK, Burns KE, Friedrich JO, Garg AX, Harel Z, Hladunewich MA, Luo J, Mamdani M, Perl J, Ray JG; University of Toronto Acute Kidney Injury Research Group: Risk of chronic dialysis and death following acute kidney injury. Am J Med 125: 585-593, 2012