



Delayed Recognition of Evolving Sepsis Following Extended Resection of Perihilar Cholangiocarcinoma: A Perioperative Anesthetic Perspective

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Abstract: Perihilar cholangiocarcinoma is associated with high perioperative morbidity because chronic biliary obstruction may conceal an evolving systemic inflammatory process before overt sepsis becomes clinically apparent. We report an elderly patient presenting with progressive jaundice, generalized pruritus, dark urine, pale stools, and significant weight loss who underwent radical resection with biliodigestive reconstruction for a Bismuth-Corlette type I tumor. Despite stable preoperative hemodynamics, persistent leukocytosis, anemia, elevated neutrophil-to-lymphocyte ratio, severe hyperbilirubinemia, hypoalbuminemia, hyponatremia, markedly elevated erythrocyte sedimentation rate, and hypouricemia suggested limited physiological reserve and possible evolving sepsis. The intraoperative course was uneventful, and early postoperative recovery appeared satisfactory. However, approximately 112 hours after surgery, the patient developed circulatory collapse with hyperlactatemia and progressive multiple organ dysfunction despite intensive care management, resulting in death on the fifth postoperative day, although blood cultures were not obtained prior to antibiotic administration and no pathogen was microbiologically confirmed. This case highlights the importance of integrating serial laboratory trends with clinical assessment, alongside prompt microbiological sampling, to facilitate earlier recognition of evolving sepsis in high-risk hepatobiliary surgery

Keywords: perihilar cholangiocarcinoma; perioperative anesthesia; sepsis; multiple organ dysfunction

INTRODUCTION

Cholangiocarcinoma is a malignant epithelial tumor of the biliary tract associated with poor prognosis and high mortality rates. Anatomically, cholangiocarcinoma is classified into intrahepatic, perihilar, and distal types, with perihilar cholangiocarcinoma (Klatskin tumor) being the most common form. Progressive biliary obstruction caused by the tumor may manifest as jaundice, pruritus, dark urine, pale stools, weight loss, and deterioration of the patient's general condition.^{1,2} In addition to impairing bile flow, biliary obstruction increases the risk of biliary tract infection, which may progress to sepsis, particularly in patients with advanced disease and poor nutritional status.³ Surgical resection remains the only potentially curative treatment for resectable disease. In perihilar cholangiocarcinoma, surgery often involves extensive hepatobiliary exploration and biliodigestive reconstruction, including Roux-en-Y hepaticojejunostomy or omega loop reconstruction.^{4,5} However, major hepatobiliary surgery is highly complex and carries substantial perioperative risks, including hemodynamic instability and postoperative sepsis, all of which contribute significantly to patient morbidity and mortality.⁶

These perioperative risks are further amplified in geriatric patients. Reduced physiological reserve, malnutrition, and functional decline limit the ability to compensate for surgical stress and infection.⁷ Furthermore, the clinical manifestations of sepsis in older adults are frequently atypical, potentially leading to delayed recognition and treatment, thereby increasing the risk of organ failure and death.⁸ This case report describes the perioperative anesthetic management of an elderly patient with perihilar cholangiocarcinoma who underwent extensive tumor resection and biliodigestive reconstruction using the omega technique, and highlights the challenges associated with recognizing the evolution of postoperative sepsis, which initially presented without clear clinical manifestations before progressing to a gradual and ultimately severe clinical deterioration.

CASE REPORT

A 64-year-old man presented with progressive obstructive jaundice accompanied by right upper quadrant abdominal pain, generalized pruritus, dark urine, pale-to-black stools, anorexia, and marked weight loss of approximately 20 kg over 2.5 months. Contrast-enhanced abdominal computed tomography demonstrated a 0.9×1.1 cm enhancing hilar lesion causing bilateral intrahepatic and extrahepatic bile duct dilatation, consistent with a Bismuth-Corlette type I perihilar cholangiocarcinoma (Klatskin tumor). Abdominal ultrasonography confirmed marked biliary dilatation without evidence of hepatic mass or intra-abdominal free fluid, while chest radiography showed no significant abnormality (Figure 1).

Preoperative laboratory evaluations (April 14, April 27, and May 5, 2026, with arterial blood gas analysis in May 23, 2026, the day before surgery) demonstrated persistent anemia, leukocytosis, hyponatremia, hypoalbuminemia, elevated liver enzymes, marked hyperbilirubinemia, a markedly elevated erythrocyte sedimentation rate, and hypouricemia despite optimization, while renal function remained preserved (Table 1). Arterial blood gas analysis performed immediately before surgery demonstrated preserved acid–base status with only mildly elevated lactate.

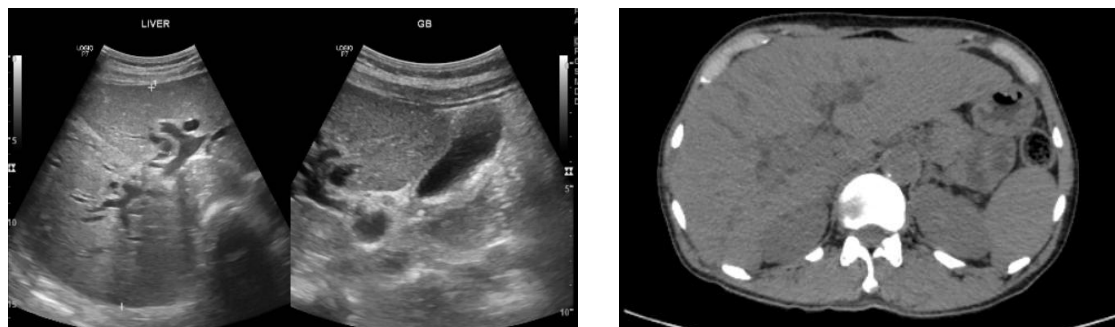


Figure 1. Preoperative abdomen USG and CT Scan with contrast

Table 1. Preoperative laboratory results by date

Parameter	Apr 14, 2026	Apr 27, 2026	May 5, 2026	May 23, 2026 (pre-op day)	Reference range	Unit
Hemoglobin	9.5 L	10.0 L	-	-	13.5–17.5	g/dL
Leukocyte count	11.8 H	17.4 H	-	-	4.5–11.0	$\times 10^3/\mu\text{L}$
NLR	4.55 H	5.21 H	-	-	<3.13	-
ESR	104 H	86 H	-	-	0–15	mm/h
PTT	-	10.6	-	-	10.1	sec
APTT	-	27.6	-	-	(control) 28.0	sec
Sodium	132.6 L	130.2 L	-	-	(control) 135–155	mmol/L
AST (SGOT)	88 H	118 H	140 H	-	10–35	U/L
ALT (SGPT)	74 H	89 H	94 H	-	9–43	U/L
Albumin	2.8 L	2.8 L	-	-	3.4–4.8	g/dL
Total bilirubin	14.44 H	-	-	-	<1.2	mg/dL
Direct bilirubin	10.98 H	-	-	-	0.2–0.4	mg/dL
Creatinine	0.8	0.9	0.77	-	0.6–1.3	mg/dL
Uric acid	2.1 L	-	-	-	3.4–7	mg/dL
Lactate (ABG)	-	-	-	1.80 H	0.9–1.7	mmol/L
pH (ABG)	-	-	-	7.44	7.35–7.45	-

On the day of surgery, the patient was hemodynamically stable with a blood pressure of 125/71 mmHg, heart rate of 86 beats/minute, respiratory rate of 20 breaths/minute, body temperature of 36.7°C, and oxygen saturation of 98% on room air. Wide tumor excision with omega-loop biliodigestive reconstruction was performed under general anesthesia. The procedure lasted 3 hours and 55 minutes with estimated blood loss of approximately 100 mL and urine output of 200 mL. During surgery, transient hypotension accompanied by sinus bradycardia (lowest blood pressure 68/46 mmHg and heart rate 58 beats/minute) occurred but responded promptly to intravenous atropine. Hemodynamic parameters subsequently remained stable throughout the remainder of the procedure (Figure 2).

The patient was extubated uneventfully one hour after surgery and transferred to the surgical ward after achieving an Aldrete score of 10. During the early postoperative period, he remained hemodynamically stable without vasopressor support (Figure 2). Serial laboratory investigations initially demonstrated partial improvement, including normalization of serum sodium, improvement of albumin concentration, reduction of serum bilirubin, and normalization of leukocyte count on postoperative day 2, although the neutrophil-to-lymphocyte ratio (NLR) remained elevated (Table 2).

However, approximately 112 hours after surgery (postoperative day 5), the patient experienced abrupt clinical deterioration characterized by dyspnea, hypotension (98/56 mmHg), tachycardia (132 beats/minute), tachypnea (28 breaths/minute), peripheral oxygen saturation (SpO_2) of 80% by pulse oximetry despite oxygen delivered via a non-rebreathing mask at 15 L/minute, and prolonged capillary refill time. Repeat laboratory evaluation revealed marked deterioration compared with previous examinations, including recurrent leukocytosis, a markedly increased neutrophil-to-lymphocyte ratio, metabolic acidosis, hyperlactatemia (4.5 mmol/L), severe hypoxemia, and acute kidney injury (creatinine 2.05 mg/dL) (Table 2), strongly suggesting evolving postoperative sepsis with multiple organ dysfunction.

The patient was transferred immediately to the intensive care unit (admitted 07:00 WIB, May 29, 2026), where norepinephrine infusion was initiated and progressively escalated because of persistent circulatory instability despite fluid resuscitation. Broad-spectrum antibiotics and supportive management were administered; however, progressive oliguria, worsening hemodynamic instability, and declining consciousness ensued. Approximately 12 hours after ICU admission, the patient developed profound bradycardia (19:40 WIB) followed by cardiac arrest.

Despite advanced cardiopulmonary resuscitation, return of spontaneous circulation was not achieved, and the patient was pronounced dead in May 29, 2026 (Figure 2).

Table 2. Postoperative laboratory results by date

Parameter	May 24, 2026 (POD0)	May 26, 2026 (POD2)	May 29, 2026 (POD5)	Reference range	Unit
Hemoglobin	9.5 L	10.6 L	11.9 L	13.5–17.5	g/dL
Leukocyte count	17.2 H	4.8	15.6 H	4.5–11.0	$\times 10^3/\mu\text{L}$
NLR	7.22 H	6.72 H	9.56 H	<3.13	-
ESR	50 H	38 H	48 H	0–15	mm/h
Sodium	136.2	140.5	138.6	135–155	mmol/L
Albumin	2.0 L	2.7 L	-	3.4–4.8	g/dL
Total bilirubin	-	10.26 H	-	<1.2	mg/dL
Direct bilirubin	-	7.86 H	-	0.2–0.4	mg/dL
Creatinine	-	-	2.05 H	0.6–1.3	mg/dL
Urea	-	-	96 H	12–43	mg/dL
BUN	-	-	45 H	6–20	mg/dL
pH (ABG)	-	-	7.37	7.35–7.45	-
pCO ₂ (ABG)	-	-	28.8 L	35–45	mmHg
pO ₂ (ABG)	-	-	42 L	83–108	mmHg
HCO ₃	-	-	17 L	22–26	mmol/L
Base excess	-	-	-6.7 L	-2 – +2	-
SO ₂ (ABG)	-	-	79 L	95–98	%
Lactate	-	-	4.50 H	0.9–1.7	mmol/L
FiO ₂	-	-	0.61	0.21	-

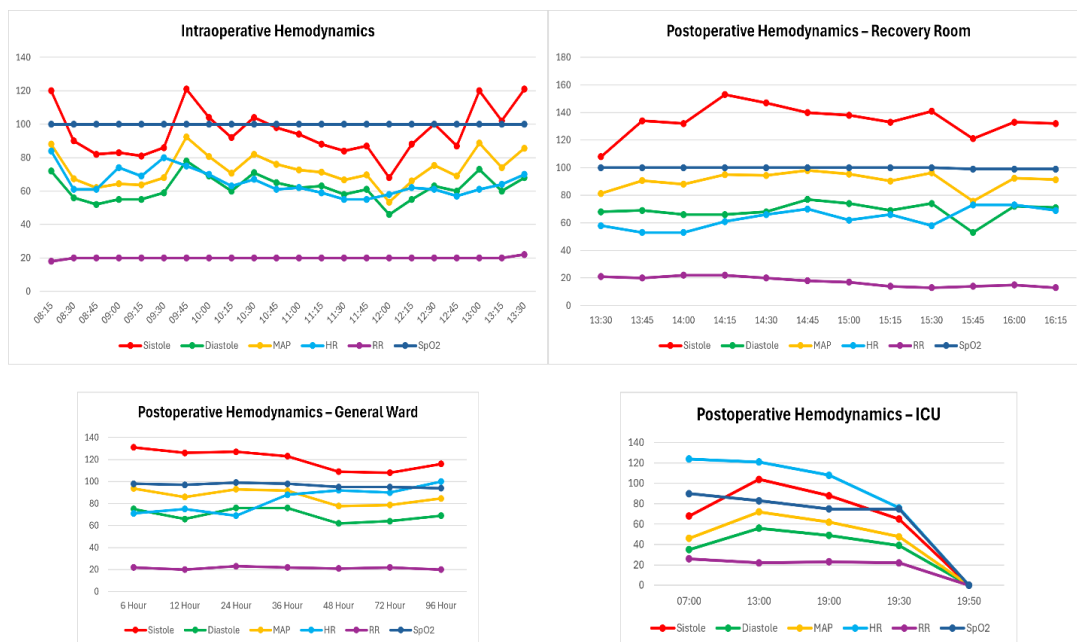


Figure 2. Patient's hemodynamics (intra and postoperative hemodynamics)

DISCUSSION

Perihilar cholangiocarcinoma is a complex hepatobiliary malignancy that is frequently accompanied by chronic biliary obstruction, cholestasis, malnutrition, and systemic inflammation, all of which substantially increase perioperative morbidity and mortality.¹ Although curative treatment requires radical resection with biliary reconstruction, major hepatobiliary surgery itself induces a significant inflammatory response that may further compromise patients with limited physiological reserve.^{9,10} In this case, surgery was technically uneventful, yet the patient developed

rapidly progressive postoperative multiple organ dysfunction and died on the fifth postoperative day. The clinical course suggests that systemic inflammation was already evolving before surgery despite apparently stable preoperative hemodynamics.

The patient presented with classical malignant biliary obstruction manifested by progressive jaundice, generalized pruritus, dark urine, pale stools, and significant weight loss. CT imaging demonstrated a Bismuth-Corlette type I tumor with marked intrahepatic and extrahepatic bile duct dilatation. Besides mechanical obstruction, prolonged cholestasis predisposes patients to bacterial colonization because impaired bile flow weakens one of the body's natural antimicrobial defense mechanisms, allowing occult cholangitis to occur even without fever or overt septic manifestations, particularly in elderly and malnourished patients.^{1,8,11} This mechanism supports the possibility that the patient had an unrecognized biliary infectious process before surgery.

Although preoperative vital signs remained stable, laboratory findings suggested markedly impaired physiological reserve. Hemoglobin remained low (9.5–10.0 g/dL), leukocyte count progressively increased (11.8 to 17.4 $\times 10^3/\mu\text{L}$), NLR remained elevated (4.55–5.21), and ESR reached 104 mm/hour, indicating persistent systemic inflammation rather than isolated biliary obstruction. Previous studies have demonstrated that preoperative leukocytosis and elevated NLR are associated with increased postoperative infectious complications and poorer outcomes in hepatobiliary malignancies.^{12–14} Furthermore, severe cholestasis was reflected by total bilirubin of 14.44 mg/dL, direct bilirubin of 10.98 mg/dL, elevated AST (88–140 U/L) and ALT (74–94 U/L), together with persistent hypoalbuminemia (2.8 g/dL). Cholestasis has been associated with impaired immune function, metabolic disturbances, coagulation abnormalities, and increased postoperative infection.^{15,16}

Several additional laboratory abnormalities further strengthened the suspicion of an evolving inflammatory process. Serum sodium remained low (130.2–132.6 mmol/L), and the erythrocyte sedimentation rate was markedly elevated (86–104 mm/hour; reference <15 mm/hour), and serum uric acid decreased to 2.1 mg/dL. Hyponatremia has been associated with systemic inflammation and poor perioperative outcomes, whereas coagulation abnormalities in obstructive jaundice mainly result from impaired vitamin K absorption secondary to cholestasis.^{15,16} Interestingly, hypouricemia has recently been proposed as an indirect marker of oxidative stress and early tissue injury because uric acid functions as an important endogenous antioxidant.¹⁷ Therefore, the coexistence of hypouricemia, leukocytosis, hypoalbuminemia, cholestasis, and malnutrition raises the possibility that tissue injury had already developed before overt organ dysfunction became clinically apparent.

Persistent hypoalbuminemia deserves particular attention because albumin is not only a nutritional marker but also maintains oncotic pressure, endothelial integrity, antioxidant activity, and drug transport. Hypoalbuminemia has consistently been associated with impaired wound healing, postoperative infection, prolonged hospitalization, and increased mortality in hepatobiliary surgery.^{18–20} Reduced albumin may also alter the pharmacokinetics of protein-bound medications, although no clinically significant anesthetic effect was observed in this patient.²¹ More importantly, persistent hypoalbuminemia likely reflected an ongoing inflammatory state and limited physiological reserve rather than nutritional deficiency alone.²²

Collectively, these findings raise an important question regarding surgical timing. Definitive management of malignant biliary obstruction requires source control through surgical resection; however, proceeding with major surgery in the presence of unresolved inflammation or occult infection may amplify the inflammatory response. This clinical course is compatible with the "second-hit phenomenon," whereby chronic inflammation from biliary obstruction constitutes the first hit and extensive surgery acts as the second insult, precipitating immune dysregulation, endothelial dysfunction, and subsequent organ failure.^{23,24}

Despite these preoperative abnormalities, the intraoperative course remained relatively stable. A transient episode of hypotension (68/46 mmHg) with sinus bradycardia (58 beats/minute) responded promptly to intravenous atropine. Blood loss was only approximately

100 mL, urine output reached 200 mL, oxygen saturation remained 100%, and vasopressor support was unnecessary. These transient hemodynamic disturbances are common during upper abdominal surgery because of anesthetic-induced cardiovascular depression and vagal stimulation.^{25–27} Therefore, intraoperative events alone were unlikely to explain the profound deterioration several days later.

The early postoperative period also appeared favorable. The patient was extubated one hour after surgery with an Aldrete score of 10 and remained hemodynamically stable for four days (surgery and postoperative day 0: May 24, 2026). Laboratory parameters initially improved: hemoglobin increased to 10.6 g/dL, leukocyte count normalized to $4.8 \times 10^3/\mu\text{L}$, sodium increased to 140.5 mmol/L, albumin improved from 2.0 to 2.7 g/dL (postoperative day 2, May 26, 2026), while total and direct bilirubin decreased to 10.26 mg/dL and 7.86 mg/dL, respectively. However, recovery was incomplete because NLR remained elevated (6.72) and albumin remained below normal despite transient improvement. Persistent postoperative inflammatory activity has previously been associated with subsequent infectious complications.²⁸ Albumin also behaves as a negative acute-phase protein; therefore, persistent hypoalbuminemia may indicate ongoing inflammation even when conventional clinical parameters appear reassuring.²²

Approximately 112 hours after surgery, the patient's condition deteriorated abruptly with hypotension, tachycardia, tachypnea, severe hypoxemia, oliguria, prolonged capillary refill time, and decreased consciousness requiring ICU admission. Laboratory evaluation simultaneously demonstrated recurrent leukocytosis ($15.6 \times 10^3/\mu\text{L}$) with NLR 9.56, compensated metabolic acidosis (pH 7.37; HCO_3^- 17 mmol/L; base excess -6.7 mmol/L; CO_2 28.8 mmHg), hyperlactatemia (4.5 mmol/L), severe hypoxemia (PaO_2 42 mmHg despite FiO_2 61%), and acute kidney injury with (creatinine 2.05 mg/dL, urea 96 mg/dL, BUN 45 mg/dL, and oliguria with a urine output of <30 mL during the 12-hour observation period). These findings indicated progressive tissue hypoperfusion and failure of multiple organ systems.²⁸

According to the sepsis definition, the combination of suspected infection with life-threatening organ dysfunction strongly supports the diagnosis of sepsis, while escalating norepinephrine requirement together with profound circulatory and metabolic abnormalities suggests progression toward septic shock.²⁹ Hyperlactatemia further indicated impaired tissue perfusion and microcirculatory dysfunction, both of which are strongly associated with poor prognosis.³⁰ Progressive vasopressor escalation from 0.1 to 0.3 $\mu\text{g/kg/min}$ without meaningful hemodynamic improvement suggested refractory vasoplegia, which carries extremely high mortality.³¹ Concurrent respiratory failure, acute kidney injury, circulatory collapse, and neurological deterioration were consistent with multiple organ dysfunction syndrome.^{32–34}

One limitation of this case is the absence of microbiological confirmation because blood cultures were not obtained before antibiotic administration. Current Surviving Sepsis Campaign guidelines recommend obtaining cultures before antimicrobial therapy whenever this does not delay treatment.²⁹ Nevertheless, failure to isolate a pathogen should not exclude the diagnosis of sepsis when progressive organ dysfunction develops in the setting of a highly suspected biliary source after major hepatobiliary surgery.

CONCLUSION

Overall, this case suggests that the patient's deterioration was not an isolated postoperative event but rather the culmination of an evolving inflammatory process that had likely begun before surgery. Preoperative anemia, persistent leukocytosis, elevated NLR, cholestasis, hypoalbuminemia, hyponatremia, markedly elevated ESR, and hypouricemia collectively indicated limited physiological reserve despite stable hemodynamics. Early postoperative laboratory improvement likely represented temporary physiological compensation rather than complete recovery. Recognition of these biological warning signs, combined with close serial laboratory monitoring and early evaluation for occult infection, may facilitate earlier diagnosis of evolving sepsis before irreversible multiple organ dysfunction develops in high-risk hepatobiliary surgical patients.

Conflict of Interest

The authors declare no conflict of interest related to the research, authorship, or publication of this article.

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