

The Use of Cangrelor as Bridge Antiplatelet Therapy in a Patient with Recent Percutaneous Coronary Intervention for Acute Coronary Syndrome, Who Developed Esophageal Perforation After Transesophageal Echocardiography

Yakın Zamanda Akut Koroner Sendrom Nedeniyle Perkütan Koroner Girişim Öyküsü Olan ve Transözofageal Ekokardiyografi Sonrasında Özofagus Perforasyonu Gelişen Bir Hastada Kangrelorun Köprü Antitrombosit Tedavisi Olarak Kullanılması

ABSTRACT

Dual antiplatelet therapy (DAPT) is a vital part of the pharmacological management in patients with coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI). While early discontinuation of DAPT increases ischemic risk, some patients on DAPT may require urgent surgery, necessitating its interruption. Cangrelor, an intravenous P2Y12 antagonist, provides strong platelet inhibition within minutes and platelet activity normalizes within one hour after the cessation of the drug. Bridging antiplatelet therapy with cangrelor has been increasingly studied as an alternative option to ensure the continuation of platelet inhibition in CAD patients who require discontinuation of DAPT. The present patient, with a recent history of PCI for acute coronary syndrome, experienced a significant esophageal perforation following transesophageal echocardiography (TEE). This severe complication was effectively managed endoscopically, and as part of the recent PCI treatment, prolonged cangrelor infusion was successfully utilized with no thrombotic or bleeding events throughout the management of the complication.

Keywords: Antiplatelet, cangrelor, esophageal perforation, transesophageal echocardiography











ÖZET

İkili antitrombosit tedavisi, perkütan koroner girişim (PKG) uygulanan koroner arter hastalığı (KAH) olan hastalarda farmakolojik tedavinin hayati bir parçasıdır. İkili antitrombosit tedavinin erken kesilmesi iskemik olay riskini artırırken, ikili antitrombosit kullanan bazı hastaların acil ameliyat gereksinimi olabilir ve bu da tedavinin kesilmesini gerektirebilir. İntravenöz bir P2Y12 antagonisti olarak Kangrelor, yalnızca birkaç dakika içinde güçlü bir trombosit inhibisyonu sağlar ve ilacın kesilmesinden sonraki bir saat içinde trombosit aktivitesi normalleşir. Kangrelor köprüleme ile uygulanan antitrombosit tedavisi, ikili antitrombosit tedavinin kesilmesini gerektiren KAH hastalarında trombosit inhibisyonunun devamını sağlamak için alternatif bir seçenek olarak giderek daha fazla çalışılmaktadır. Akut koroner sendrom nedeniyle yakın zamanda PKG öyküsü olan hastamızda, transözofageal ekokardiyografi (TEE) sonrasında ciddi bir özofagus perforasyonu yaşandı. Bu ölümcül komplikasyon endoskopik olarak iyi bir şekilde yönetildi ve yakın zamanda uygulanmış PKG tedavisinin bir parçası olarak uzatılmış kangrelor infüzyonu, komplikasyonun yönetimi boyunca hiçbir trombotik veya kanama olayı olmaksızın başarıyla kullanıldı.

Anahtar Kelimeler: Antitrombosit, kangrelor, özofageal perforasyon, transözofageal ekokardiyografi

CASE REPORT

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Dual antiplatelet therapy (DAPT) is the cornerstone of pharmaceutical treatment for patients with coronary artery disease undergoing percutaneous coronary intervention (PCI), especially within the first three months post-PCI.¹ Early cessation of DAPT is associated with a significantly increased risk of major ischemic and thrombotic

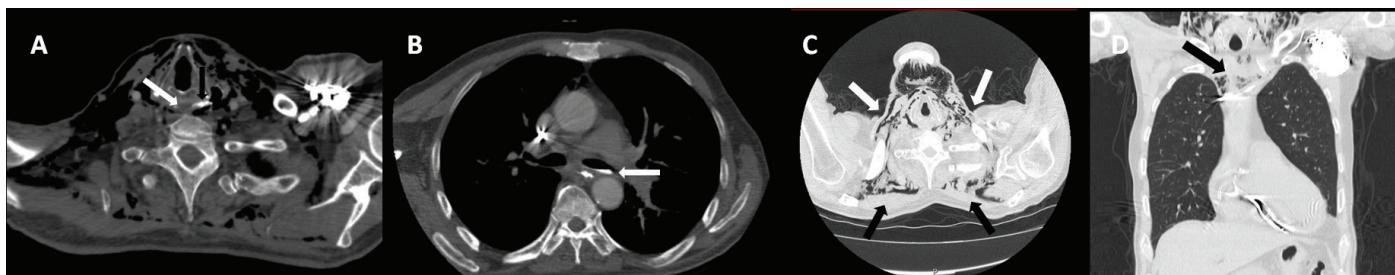


Figure 1. Thorax and cervical computed tomography (CT) scan images. Leakage of contrast agent (black arrow) indicates cervical esophagus perforation (white arrow) (A). Contrast agent in the left main bronchus (white arrow) shows fistulization of the esophagus perforation into the airway (B). Subcutaneous emphysema in the cervical area (white arrows) and back (black arrows) (C). Pneumomediastinum (black arrow) (D). CT, Computed Tomography.

cardiovascular events.¹ Nonetheless, certain clinical scenarios may necessitate the interruption of DAPT, such as when a patient requires urgent surgery. Cangrelor, an intravenous, reversible P2Y₁₂ antagonist, provides 90% platelet inhibition within minutes, with platelet activity normalizing within one hour after discontinuation.² The infusion of cangrelor is generally maintained for at least two hours or throughout the duration of the PCI procedure, whichever is longer.² This agent is particularly beneficial for patients who cannot be pre-treated with a P2Y₁₂ inhibitor due to the inability to use the gastrointestinal route, notably intubated patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI.² Additionally, literature reports exist on the off-label use of cangrelor.³⁻⁵ Typically, these cases involve patients with a recent history of PCI who require urgent non-cardiac or cardiac surgical procedures.

Esophageal perforation is an extremely rare and life-threatening complication of transesophageal echocardiography (TEE) that demands immediate diagnosis and a multidisciplinary treatment approach.⁶ While the primary management of this complication involves complex, high-risk surgery, endoscopic procedures may serve as an alternative for select high-risk patients.⁶ However, it is crucial to consider that the endoscopic method can pose significant limitations, including a potentially extended inability to utilize the gastrointestinal route. We describe a case in which an extended cangrelor infusion was implemented in a patient on DAPT who had undergone PCI with the placement of two drug-eluting stents (DES) two weeks prior. This patient was unable to use the gastrointestinal route for a week due to a severe esophageal perforation incurred following a TEE procedure.

Case Report

A 67-year-old man presented with generalized malaise, fever, and chills over the past two days. Upon admission, his

temperature was 38.2 °C with a heart rate of 104 beats per minute. His blood pressure measured 124/68 mmHg, and his oxygen saturation was 96% on room air. The physical examination was unremarkable. The patient had a medical history of ischemic cardiomyopathy, intracardiac defibrillator (ICD) implantation, chronic renal disease, and chronic obstructive pulmonary disease. Two weeks prior, he was hospitalized for acute coronary syndrome (ACS) and underwent PCI with the implantation of two DES in the proximal segments of the right coronary artery and left anterior descending artery. Laboratory tests showed an elevated C-reactive protein level (133 mg/L; reference: <5 mg/L), increased sedimentation rate (49 mm/h; reference: <20 mm/h), leukocytosis, and a reduced estimated glomerular filtration rate (46 mL/min/1.73 m²). Other laboratory results were within normal limits. The electrocardiogram (ECG) displayed nonspecific changes, and the chest X-ray showed no signs of acute pathology. Transthoracic echocardiography revealed a suspected small oscillatory mass on the ICD lead. However, TEE did not demonstrate any signs of infective endocarditis on the lead or elsewhere in the heart. Post-TEE, the patient developed sudden severe throat pain, dysphagia, and dyspnea. Thoracic and cervical computed tomography (CT) scan identified a massive upper esophageal perforation, pneumomediastinum, and subcutaneous emphysema (Figure 1A-D). A multidisciplinary team, including thoracic surgeons, general surgeons, clinical cardiologists, gastroenterologists, and anesthesiologists, evaluated the case to determine the management strategy for this life-threatening complication. Given the patient's significant perioperative mortality risk due to his severe comorbidities, endoscopic management was recommended, and consent was obtained. During esophagogastroscope, multiple esophageal perforation sites were identified (Figure 2A-B). A temporary fully covered graft-stent (20 x 80 mm, Micro-Tech) was successfully implanted, closing the perforated segments effectively (Figure 2C). Following the endoscopic procedure, the gastroenterologists strongly advised against the insertion of nasogastric or orogastric tubes and any use of the gastrointestinal route to prevent potential damage to the esophagus. The patient remained intubated under general anesthesia without any utilization of the gastrointestinal route until the scheduled follow-up endoscopy, which was set for one week later. During this period, it was crucial to effectively manage the patient's antiplatelet therapy to prevent the risk of subacute stent thrombosis,

ABBREVIATIONS

ACS	Acute coronary syndrome
CAD	Coronary artery disease
CT	Computed tomography
DAPT	Dual antiplatelet therapy
DES	Drug-eluting stents
ICD	Intracardiac defibrillator
PCI	Percutaneous coronary intervention
STEMI	ST-segment elevation myocardial infarction
TEE	Transesophageal echocardiography

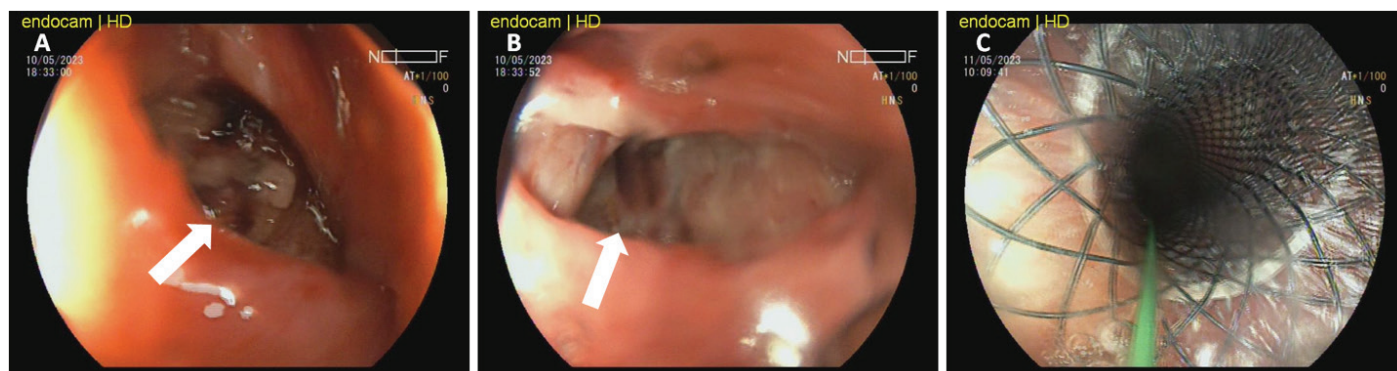


Figure 2. Endoscopy images. Segments of esophageal perforation (white arrows) (A, B). The perforated esophagus is successfully closed with a temporary full covered graft-stent (C).

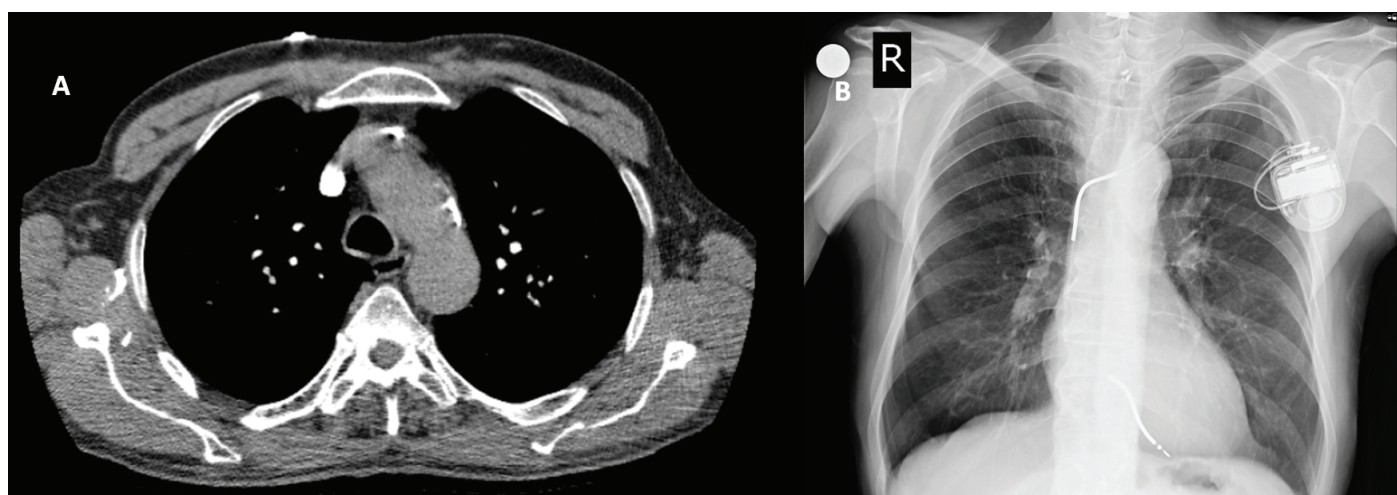


Figure 3. Control CT and chest X-ray images after one month. CT shows complete closure of the esophageal perforation (A). The control chest X-ray reveals complete resolution of subcutaneous emphysema and pneumomediastinum (B). CT, Computed Tomography.

especially considering the recent PCI. Therefore, a bridging dose regimen of cangrelor infusion (0.75 mcg/kg/min without a bolus) was initiated on the third day of the intubation period and continued until one hour before the follow-up endoscopy. The control endoscopy a week later showed complete closure and endothelialization of the previously perforated esophageal segments. Consequently, the graft-stent was successfully removed. However, cangrelor infusion was resumed at the same dosage one hour after the control endoscopy. The patient was successfully extubated the following day and was able to tolerate an oral diet. Subsequently, the cangrelor infusion was discontinued, and a loading dose of 300 mg clopidogrel and 300 mg aspirin was administered immediately thereafter. Throughout the management period, there were no observed changes in ECG, elevations in cardiac enzymes, or bleeding complications. The patient was discharged on optimal medical therapy including DAPT. One month post-discharge, the patient remained asymptomatic and was managing well on the oral regimen. Follow-up CT scan and chest X-ray performed one month later showed no evidence of residual perforation, fistulae, subcutaneous emphysema, or pneumomediastinum (Figure 3A-B).

Discussion

Our case involved a patient who developed esophageal perforation following a TEE procedure and was effectively managed endoscopically. Beyond addressing this life-threatening mechanical complication, it was imperative to manage the patient's antiplatelet therapy to prevent thrombotic coronary events, especially since the patient had undergone PCI with the implantation of two DES for ACS just two weeks earlier. We utilized a cangrelor infusion as a bridging antiplatelet agent without encountering any bleeding or ischemic complications during the patient's management period. Cangrelor, an intravenous and reversible P2Y₁₂ inhibitor, provides rapid and strong platelet inhibition with a quick offset.² Following the discontinuation of cangrelor infusion, it is recommended to administer an oral P2Y₁₂ inhibitor to maintain platelet inhibition.²

Another critical aspect highlighted in our case report is the life-threatening complication of esophageal perforation during TEE. The cervical esophagus is most frequently affected, with contributing factors including neck extension, the presence of anterior vertebral osteophytes, and stretching of the mucosa and muscular fibers.⁷ Shearing forces, prolonged flexion of the

probe tip, and mobilization of the probe in a locked position can contribute to esophageal tearing.⁷ Compared to perforations in other segments of the esophagus, those in the cervical esophagus generally have a more favorable prognosis.⁸ Managing esophageal rupture requires a multidisciplinary approach, incorporating surgical interventions, endoscopic procedures, conservative management, and close monitoring in an intensive care setting. The literature contains numerous case reports of esophageal perforation following TEE procedures. One such example describes a patient who sustained an esophageal perforation during a TEE examination and was managed conservatively for seven days, resulting in significant improvements.⁸ In another case, a patient with a 2 cm esophageal perforation following TEE underwent cervicotomy to drain pus from the upper mediastinum and periesophageal space.⁹ After supportive care, the patient's clinical status improved, although an esophageal fistula was still present.⁹ In our specific case, the perforation occurred at the cervical esophagus, likely during the initial probe insertion attempt. Our experienced gastroenterology team performed an endoscopic approach to the perforation site and inserted a graft stent. After seven days, the stent was successfully removed, and the patient demonstrated clinical improvement without any signs of a fistula or remaining perforation.

Cangrelor was initially approved for use in PCI when patients could not take a P2Y12 inhibitor due to intubation, shock states, or gastrointestinal issues. However, recent studies and cases have reported off-label use of cangrelor.^{2–5} Rossini et al.¹⁰ investigated the real-world use of cangrelor as an alternative antiplatelet agent in patients who had recently undergone PCI and needed to discontinue DAPT for urgent noncardiac surgery. Their findings demonstrated that no ischemic or hemorrhagic events occurred following the surgery.¹⁰ The Bridge study¹¹ was conducted to assess the reliability of using cangrelor as a bridging strategy in patients undergoing major cardiac surgery. Bleeding and thrombotic events were similar between the cangrelor group and the placebo group.¹¹ Additionally, there was no statistically significant difference in the incidence of major bleeding associated with coronary artery bypass grafting (CABG) between the cangrelor group and the placebo group (11.8% vs. 10.4%, respectively), suggesting that cangrelor can be safely used in the CABG setting.¹¹ A case report described a patient on DAPT following DES implantation who required a bronchoscopy with biopsy due to suspected lung cancer.³ Cangrelor bridge therapy was used without any complications, enabling the patient to proceed with radiation therapy following a confirmed lung cancer diagnosis.³ Some authors have documented a successful case of transitioning from ticagrelor to cangrelor infusion in orthotopic heart transplantation, with no reported complications.⁴ Furthermore, a mini case series highlighted the safety of cangrelor in three patients with STEMI who received a cangrelor infusion prior to coronary angiography.⁵ Despite all three patients being diagnosed with extensive multi-vessel disease necessitating urgent CABG surgery, there were no instances of major bleeding during the perioperative period, and all patients experienced rapid recovery.⁵ It is also worth noting that cangrelor has been administered in cases involving intracranial stent or coil implantation and acute ischemic stroke

in neurosurgical patients.^{12,13} Nonetheless, there is a need for prospective, randomized-controlled, multicenter, and large-scale studies to further investigate the application of cangrelor in both neurointervention and interventional cardiology.

Conclusion

Cangrelor, an intravenous and reversible P2Y12 antagonist, provides strong platelet inhibition within minutes, and platelet activity normalizes within one hour after the cessation of infusion.² Therefore, cangrelor has been proposed as a valuable bridging antiplatelet agent for patients who temporarily cannot use the gastrointestinal route and have an absolute need for antiplatelet therapy.² Our patient, who suffered from esophageal perforation following TEE and had recently undergone PCI with the implantation of two DES due to ACS, was successfully treated with endoscopy and a prolonged cangrelor infusion, without experiencing any thrombotic or bleeding complications.

Informed Consent: Written consent was obtained from the patient to include case details and other personal information.

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