

Coronary stent infection: a systematic review

I Gde Rurus Suryawan^a, Kevin Luke^b, Rafiv Fasya Agustianto^b and Eka Prasetya Budi Mulia^a

Coronary stent infection (CSI) is the rarest complication associated with the percutaneous coronary intervention, occurring in less than 0.1% of cases. So far, all reported instances are limited to case reports. CSI presents itself in various, often confusing, ways in clinical settings. Therefore, the current systematic review summarizes reports of CSI's clinical presentations, causative pathogens, diagnoses and treatments. This systematic review considered three online databases, using reference lists as an additional source. All case reports or case series with stent infection in the coronary artery were included – however, reviews or commentaries, articles not published in English, and articles mentioning a history of hemodialysis or any surgery were excluded. Thirty-two studies on 34 CSI patients were included in the final qualitative analysis. CSI predominantly affected males of a wide range of ages. The most common symptoms were chest pain and fever with various onsets. Interestingly, CSI usually occurred during the first stent implantation. Cultures and coronary angiography were the most common methods used to diagnose CSI. Furthermore,

drug-eluting stents had a higher risk of infection than bare-metal stents. Aneurysms were the most frequent abnormalities observed in infected stents. The bacteria that most often caused CSI were *Staphylococcus aureus* and *Pseudomonas aeruginosa*. More than 90% of the reports mentioned using various antibiotics, and 74% mentioned carrying out surgery. Finally, a mortality rate of 26.47% among CSI patients was calculated. *Coron Artery Dis XXX: 000–000* Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

Coronary Artery Disease XXX, XXX:000–000

Keywords: coronary artery disease, coronary stent complication, coronary stent infection, percutaneous coronary intervention

^aDepartment of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo General Hospital and ^bFaculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Correspondence to I Gde Rurus Suryawan, MD, PhD, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Airlangga – Dr. Soetomo General Hospital, Jl. Mayjen Prof. Dr. Moestopo No.6-8, Surabaya 60286, Indonesia
Tel: +62813 2050 0099; e-mail: igde.rurus.s@fk.unair.ac.id

Received 1 May 2021 Accepted 8 August 2021

Introduction

Coronary artery disease (CAD) is a major global health problem, as an estimated 126 million individuals worldwide are reported to suffer from CAD. In addition, CAD was responsible for 9 million deaths in 2017 [1]. Percutaneous coronary intervention (PCI) is well-recognized as a transformative CAD treatment first performed (balloon angioplasty) in 1977 by Andreas Grüntzig [2]. Since then, many advanced techniques and instruments have augmented this treatment, most notably the implantation of bare-metal stents (BMSs) to multiple generations of drug-eluting stents (DESs).

Complications rarely arise during PCI but are life-threatening when they occur. Complications such as the no-reflow phenomenon and stent thrombosis occur in about 2% of cases, while coronary stent infection (CSI) occurs in less than 0.1% of cases (all such instances are limited to case reports) [3]. The first report of a CSI case described a Palmaz-Schatz-stent infection in a 66-year-old woman in 1993 [4]. The patient died despite undergoing emergency cardiac surgery. A previous study that reviewed 23 cases demonstrated that the mortality rate of CSI was 39% [5]. Moreover, CSI has various clinical presentations that are often confusing. Therefore, this study systematically

reviews the clinical presentation, causative pathogens, diagnoses and treatments associated with reported CSI cases.

Materials and methods

Study design

We performed this systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. This systematic review is registered in the university hospital medical information network (UMIN) with registration number UMIN000043308.

Literature search

A literature search was conducted on three online databases (PubMed, ScienceDirect and ProQuest) using the keywords 'coronary stent infection' and 'stent infection.' The reference lists of both included and excluded studies were also screened for additional relevant studies.

Inclusion and exclusion criteria

Relevant full-text articles were assessed on the basis of the inclusion and exclusion criteria. Specifically, case reports or case series with stent infection in the coronary artery were included, while (1) reviews or commentaries,

(2) articles not published in English and (3) articles mentioning a history of hemodialysis or any surgery were excluded.

Data extraction and analysis

From the included articles, two independent reviewers directly extracted data regarding the authors, publication year, location, patient(s) demographics, initial presentation, onset after the procedure, involved vessel and any angiography abnormalities, type of stent, pathogen involved, treatment approaches and outcomes. The collected data are presented descriptively on the basis of baseline characteristics, clinical presentation, diagnostic methods, stent and vessel pathology, causative pathogens, management and outcomes.

Results

Selected studies and baseline characteristics

Initially, 571 articles were screened. Of these, 32 studies involving a total of 34 CSI patients were included in the analysis (Fig. 1). The earliest included case was reported by Leroy *et al.* (1996) in France [6]. Although the first-known CSI case was reported in 1993 by Günther *et al.*, this case was not included in the present review because the full-text article could not be accessed. Most cases were reported in India, and most patients were males (88.24%), with ages ranging from 38 to 86 years old (Table 1).

Clinical presentations

The clinical presentations of CSI vary among cases. Most cases reported fever (76.47%) and chest pain (52.94%) as primary symptoms, followed by shortness of breath (11.76%). Additionally, Zateyshchikov *et al.* [26] and Dalal *et al.* [29] reported cardiogenic shock and cardiac arrest, respectively, upon the admission of the CSI case.

The onset of symptoms usually occurred within the first week after stent implantation. The earliest onset of CSI occurred 1-day postprocedure, while the latest onset occurred around seven years after the procedure [23,26]. The number of stent implantation procedures performed on patients ranged from one to three. Interestingly, most CSI cases resulted from the first stent implantation (67.65%).

Diagnostic methods

Blood culture (79.41%) and coronary angiography (70.59%) were the most preferred diagnostic methods reported. Some cases in which stent or pericardial fluid evacuation were conducted also involved tissue or pericardial fluid culture to confirm pathogenic causes. Some reports also utilized a PET-CT scan and cardiac CT scan. In some instances, cardiac MRI and gallium SPECT were performed for CSI diagnosis. One postmortem study revealed coronary occlusion via an abscess [26]. Nineteen of 34 cases were definitively diagnosed by a surgical specimen or postmortem examination; the other

15 cases were confirmed by their fulfillment of Dieter's diagnostic criteria [38] (Table 2).

Stents and coronary abnormalities

DESs were the most commonly reported stents (67.65%), followed by BMSs (20.59%) and DES-BMS combination (5.88%). Two case reports did not specify the stent type. CSI occurred in the left anterior descending artery (LAD) in 21 cases and in the right coronary artery (RCA) in 14 cases. CSI in the left circumflex artery and left main coronary were rarely reported.

Twenty-nine reports describe abnormalities in coronary morphology, with aneurysm (true- and pseudoaneurysm) being the most common (64.71%), followed by vessel occlusion (32.35%) and in-stent restenosis (20.59%). Coronary-cameral fistula, coronary perforation and soft-tissue density collection were also reported.

Causative pathogens

All CSI pathogens identified in the current review were bacteria. *Staphylococci* bacteria were the most prevalent pathogens, of which *Staphylococcus aureus* was the most commonly reported. Out of 17 reports, seven cases included methicillin-resistant *Staphylococcus aureus*. *Pseudomonas aeruginosa* were also prevalent, while *Acinetobacter baumannii*, *Escherichia coli*, *Enterobacter cloacae*, and *Actinomyces oris* were reported in few cases. Bacterial cultures did not grow in two cases – these cases described a history of *Staphylococcus aureus* bacteremia 2 and 3 months before surgery, with one case traced back to rare gram-positive cocci [12,15].

Treatments, complications and outcome

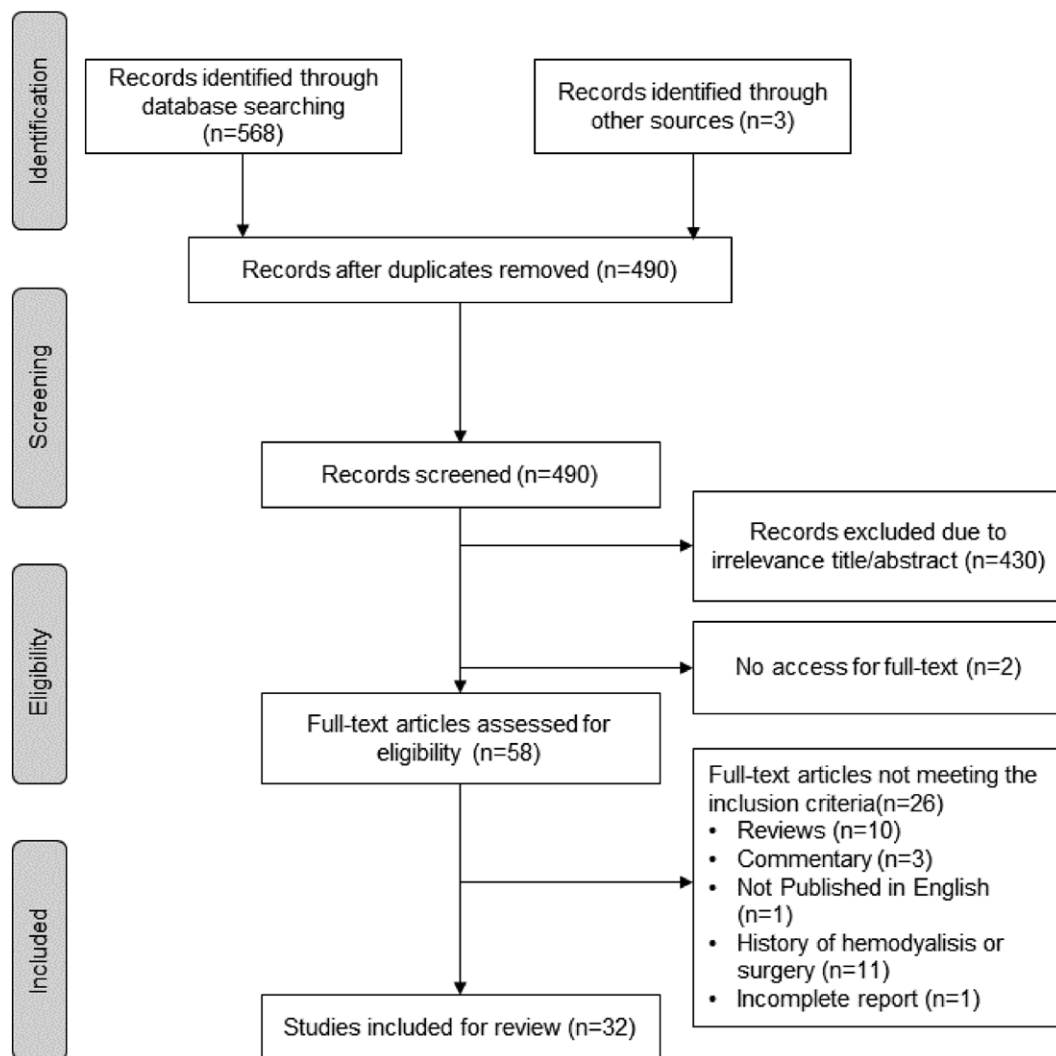
Antibiotic therapy was mentioned in 31 cases. One study did not mention giving any antibiotics, while another was a postmortem study. Meanwhile, surgery was performed in only 26 cases. Table 3 provides detailed information related to the antibiotics administered and the surgeries performed. Pericardial effusion, abscess, heart failure and valvular involvement were the most often reported complications. The results demonstrate a mortality rate of 26.47% among CSI patients.

Discussion

This systematic review addresses 34 CSI cases from 32 reports. CSI predominantly affected males of a wide range of ages. The most common symptoms were chest pain and fever, the onset of which varied among cases. Interestingly, most CSI cases occurred during the first stent implantation. Cultures and coronary angiography were the most common methods used to diagnose CSI, though some cases also reported more advanced imaging modalities.

The majority of infected stents were DESs placed in the LAD or RCA. Furthermore, aneurysms were the most common abnormalities found in infected stents, followed

Fig. 1



Systematic search and screen flowchart.

by vessel occlusion and in-stent restenosis. Pathogenic agents commonly caused bacteria, namely *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Hence, more than 90% of the cases mentioned using various antibiotics, while 74% of the cases involved surgery. In addition, our systematic review presented a mortality rate of 26.47% among CSI patients.

Our findings are similar to a previous review of 25 coronary infection cases carried out by Franco *et al.* [5]. Their review included patients with balloon-related and saphenous vein graft stent infections and showed that the most common symptoms were fever, chills and chest pain. These symptoms occurred two days to 4 months post-intervention.

In addition, coronary angiography was the most preferred diagnostic modality. The prevalence of infection in DESs was slightly higher than in BMSs (48% vs.

32%), and the most common causative pathogens were *Staphylococcus aureus* (80%) and *Pseudomonas aeruginosa* (20%). Surprisingly, the recorded CSI mortality rate was 39% after excluding balloon-related infections. Another review of 17 cases demonstrated similar results but did not address the type of stents used [39].

The pathophysiology of CSI remains unclear. Stent implantation, specifically as it relates to its struts, disrupts coronary endothelial surface and impairs the host defense mechanism. The stent itself serves as an ideal reservoir for bacterial growth [5]. Moreover, increasing the popularity and use of DESs is associated with a higher incidence of CSI. The immunosuppressive effect of eluted drugs inhibits restenosis via neointima growth and hyperplasia suppression while also reducing the protective function of neointima against infection [40].

Table 1 Summary of coronary stent infection cases

Author	Sex	Age	Presenting Symptoms	First onset	N of PCI	Diagnostic methods	Stent type	Vessel	Angiographic abnormality	Pathogen	Complication	Outcome
Leroy et al. France (1996) [6]	M	49	F	1 week	1	BC, CAG, TC, Urine Culture	BMS	LAD	Saccular aneurysm	<i>P. aeruginosa</i>	Vi, IE	Died
Bouchart et al. France (1997) [7]	M	38	CP	6 days	1	BC, CTC, TC	BMS	LCX	Pseudoaneurysm, VO	<i>P. aeruginosa</i>	PE, partial aneurysm rupture	Survived
Grewe et al. Germany (1999) [8]	M	54	CP, F	4 days	1	BC, TC, Autopsy	BMS	LAD	-	<i>S. aureus</i>	VF, HF, suppurative pancarditis	Died
Liu et al. USA (2003) [9]	M	72	CP, F	18 days	1	BC, CAG, TC	BMS	LAD	Pseudoaneurysm	<i>S. aureus, S. simulans, S. capitis</i>	S. Abscess	Survived
Hoffman et al. Israel (2005) [10]	M	80	CP, F	1 week	1	BC, CTC	DES	LAD	Soft-tissue mass	<i>S. aureus</i>	Lung and Liver Abscess, Bacterial Endophthalmitis	Survived
Alfonso et al. Spain (2005) [11]	M	47	CP, F	2 days	2	BC, PFC	DES	RCA	-	<i>S. aureus</i>	PE, Hemopericardium	Died
Marcu et al. USA (2005) [12]	M	55	F	3 months	1	BC, CAG, Tissue Gram Staining	DES	LAD	Pseudoaneurysm ISR	History of <i>S. aureus</i> , Rare Granulation Gram-positive cocci		Survived
Singh et al. India (2005) [13]	M	56	F, SoB	4 days	1	BC, CAG	DES, BMS	LAD, RCA	Saccular aneurysm, ISR	<i>S. aureus</i>	-	Survived
Garg et al. USA (2007) [14]	Fm	86	CP	>9 days	1	BC, CAG	DES	LAD, RCA	Mycotic aneurysm, Coronary perforation	MRSA	PE	Died
Kishida et al. Japan (2007) [15]	M	70	F	2 months	2	CAG, TC, CTC	DES	RCA	VO, aneurysm-fistula	no growth, history of <i>S. aureus</i> bacteremia	Microabscess	Survived
Schoenkerman and Lundstrom, USA (2009) [16]	M	59	F	4 days	1	BC, CAG, Urine Culture	BMS	LAD	Mycotic aneurysm	<i>S. aureus</i>	Aneurysm rupture, HF/EF, Shock, Lung Edema	Died
Lim et al. Singapore (2011) [17]	M	69	F	4 days	2	BC, CAG, CTC	DES	LAD	Pseudoaneurysm	MRSA	Low Cardiac Output Syndrome	Died
Furtado et al. India (2011) [18]	M	62	CP, F	2 weeks	1	BC, CAG, TC	DES	LAD	Pseudoaneurysm	<i>P. aeruginosa</i>	Abscess, PE	Survived
Patel et al. USA (2013) [19]	M	60	CP, SoB	8 weeks	1	PFC, CAG	DES	LAD	Mycotic aneurysm	MRSA	PE	Survived
Morris et al. UK (2013) [20]	Fm	ND	F	5 days	1	BC, Echo	ND	LM-LAD	-	<i>S. lugdunensis</i>	Abscess, PE	Died
Wedekind et al. Germany (2013) [21]	M	80	F	3 weeks	2	BC, PET-CT, PFC	DES	LAD, LCx	-	<i>E. coli</i>	PE	Survived
Chang et al. Taiwan (2013) [21]	M	38	CP	>1 year	>1	BC, CTC	ND	LM-LAD	Mycotic aneurysm	<i>S. aureus</i>	Multiorgan failure	Died
Satish et al. India (2015) [23]	ND	51	CP, F	2 days	1	BC, CAG	DES	LAD	Pseudoaneurysm	<i>Staphylococcus</i>	Abscess	Survived
Roubelakis et al. UK (2015) [24]	M	62	CP, F	3 years	1	BC, CAG, TC	DES	LAD	Aneurysm	<i>S. aureus</i>	Ruptured Aneurysm, PE	Survived
Sekhar et al. India (2015) [25]	M	60	F	15 days	1	BC, CAG, TC, FDG-PET-CT Scan	DES	RCA	ISR-VO	<i>P. aeruginosa, Enterobacter cloacae</i>	Abscess, Vi, PE	Survived
Zateyshchikov et al. Russia (2015) [26]	M	45	Cardiac Shock	7 years	1	Autopsy	BMS	RCA	-	ND	Abscess-VO	Died
Madkaiker et al. India (2016) [27]	M	50	F	4 days	2	BC, CAG, TC	DES	LAD, LCx	Pseudoaneurysm, ISR	<i>P. aeruginosa</i>	HF/EF, Lung Edema	Survived
Aggarwal et al. India (2016) [28]	M	51	CP, F	>13 month	2	TC, CTC	DES	LAD	Pseudoaneurysm, VO	<i>Pseudomonas</i>	Vi, HF/EF, non-sustained VT	Survived
Dalal et al. India (2017) [29]	Fm	66	CP	1 month	1	CAG, TC	DES	RCA	Aneurysm, VO	<i>P. aeruginosa</i>	Septic shock, AF, HF/EF,	Survived
	M	50	F, Cardiac Arrest	1 months	1	CAG, TC	DES	LCx	Aneurysm, VO	<i>P. aeruginosa</i> and <i>S. warneri</i>	HF	Survived

(continued)

Table 1 (continued)

Author	Sex	Age	Presenting Symptoms	First onset	N of PCI	Diagnostic methods	Stent type	Vessel	Angiographic abnormality	Pathogen	Complication	Outcome
Elder et al. Australia (2017) [30]	M	50	CP, F	2 days	2	BC, CAG, Gallium-SPECT	DES, BMS	RCA	VO	MRSA	Pleural effusion, PE	Survived
Sangolkar et al. India (2018) [31]	M	66	F	3 years	2	BC, CAG, PET-CT	DES	RCA	Coronary-cameral fistula	<i>P. aeruginosa</i>	Abscess, VI, Sepsis, Lymphadenopathy	Survived
Shetty et al. India (2018) [32]	M	52	CP, F	9 months	1	BC, CAG, TC, CTC	DES	RCA	Aneurysm, VO	<i>Acinetobacter baumannii</i> , <i>Staphylococcus aureus</i>		Survived
Shah et al. India (2018) [33]	M	53	F	2 years	1	TC, PET Scan, CMRI, Echo	DES	LAD	ISR	<i>P. aeruginosa</i>	Abscess, HFREF	Survived
Sudhakar, India (2018) [34]	M	49	F, SoB	2 weeks	1	BC, CAG	DES	LAD	Fusiform Aneurysm, ISR	Suspect <i>P. aeruginosa</i>	VI, IE	Survived
Messaoud et al. Tunisia (2019) [35]	M	71	CP, F	12 days	1	BC, CAG, CTC	BMS	RCA	Mycotic aneurysm, ISR	<i>S. aureus</i>	RBBB, IE, VI, PE	Survived
Reddy et al. India (2019) [36]	M	50	CP, F, SoB	8 days	3	BC, CAG, TC, PFC	DES	LAD, RCA	Aneurysm, VO	MRSA	HFREF, PE	Survived
	M	52	F	1 month	1	BC, CAG, TC, CTC, PET, PFC	DES	RCA	Pseudoaneurysm, VO	MRSA	AV block, HFREF, PE, Granulation	Survived
Saeed et al. Qatar (2020) [37]	M	50	CP	3 months	2	BC, CAG, CMRI	DES	RCA	VO	<i>Actinomyces oris</i>	Abscess	Survived

BC, blood culture; BMS, bare-metal stent; CAG, coronary angiography; CMRI, cardiovascular MRI; CP, chest pain; CTC, CT-Scan cardiac/coronary; DES, drug-eluting stent; F, fever; FDG, ¹⁸F-fluorodeoxyglucose; Fm, female; HFREF, heart failure reduced ejection fraction; IE, infective endocarditis; ISR, in-stent restenosis; M, male; MRSA, Methicillin-resistant *Staphylococcus aureus*; ND, no data; PE, pericardial effusion; PFC, pericardial fluid culture; SoB, shortness of breath; SPECT, single-photon emission computed tomography; TC, tissue culture; VI, valvular involvement; VO, vessel occlusion.

Aneurysms are commonly observed in CSI cases. Although the underlying mechanism is unknown, infected aneurysms are formed through arterial injury and direct infection – this is known as the ‘two-hit’ hypothesis [41]. The first hit strikes and the coronary artery wall, weakening it and leading to its degeneration. The first hit could be induced by atherosclerosis, trauma, coronary manipulation, infection or vascular inflammation. Subsequently, the second hit, which involves infectious materials, strikes the weakened arterial wall, thus facilitating rapid aneurysmal development.

Several methods have been utilized to diagnose CSI, with blood culture and coronary angiography being the most common. Nevertheless, previous reviews focus on the use of imaging modalities to diagnose CSI. These reviews agree that coronary angiography is the modality of choice for diagnosing CSI [5,39,40]. In the present review, we did not consider echocardiography as a diagnostic modality since it is primarily used to evaluate cardiac valve function, detect pericardial effusion, or rule out endocarditis. Additionally, transesophageal echocardiography is positive in only four out of 10 cases, whereas coronary angiography is positive in 10 out of 10 cases [39].

Currently, there is no universal standard for diagnosing CSI. However, Dieter proposed several criteria for diagnosing CSI cases [38]. A definitive diagnosis of CSI was on the basis of surgical specimens or postmortem examinations, revealing an infected coronary artery stent complex. Subsequently, three or more of the following conditions indicate CSI: (1) coronary stent implantation within the last 4 weeks, (2) repeated procedures through the same vascular sheath or complications at the puncture site, (3) bacteremia, (4) a fever above 101.5°F without any bacterial infection, (5) leukocytosis without any infection or acute coronary syndrome, (6) acute coronary syndrome, (7) cardiac imaging supporting the presence of persistent inflammation.

The classification of CSI has been proposed on the basis of its onset as adapted from orthopedic surgery [39]. Infections occurring within 10 days of stent implantation are classified as early-onset; otherwise, it is classified as late-onset.

Ideally, CSI should be treated with a combination of antibiotics and surgery. However, in some cases, treatments with antibiotics alone were effective [10,21,35]. Contrarily, several cases treated with antibiotics alone showed a different outcome [14,16,20]. Surgery is the logical treatment of choice for treating CSI, as surgery can provide a definitive diagnosis of CSI while also removing the infection source, repairing aneurysms, and providing bypass vascular grafts. However, patients often refuse surgery or die during surgery preparations [10,16].

Table 2 Case diagnosis on the basis of previous criteria [38]

Author	Sex	Age	Definitive Dx of CSI		Possible Dx of CSI							Definitive/possible diagnosis	
			Surgical specimen	Postmortem	1	2	3	4	5	6	7		
Leroy et al. France (1996) [6]	M	49	No growth	-	Yes	-	Yes	-	Yes	-	-	-	Possible
Bouchart et al. France (1997) [7]	M	38	Yes	-	Yes	-	Yes	-	Yes	-	-	Yes	Definite
Grewe et al. Germany (1999) [8]	M	54	-	Yes	-	Yes	-	Yes	-	-	Yes	-	Definite
Liu et al. USA (2003) [9]	M	72	Yes	-	Yes	-	Yes	-	Yes	-	-	-	Definite
Hoffman et al. Israel (2005) [10]	M	80	-	-	Yes	-	Yes	-	Yes	-	-	Yes	Possible
Alfonso et al. Spain (2005) [11]	M	47	-	-	Yes	-	Yes	-	Yes	-	-	Yes	Possible
Marcu et al. USA (2005) [12]	M	55	Yes	-	-	-	Yes	-	Yes	-	Yes	Yes	Definite
Singh et al. India (2005) [13]	M	56	-	-	Yes	-	Yes	-	Yes	-	Yes	Yes	Possible
Garg et al. USA (2007) [14]	Fm	86	-	-	Yes	-	Yes	-	Yes	-	Yes	Yes	Possible
Kishida et al. Japan (2007) [15]	M	70	Microabscess but no growth	-	-	-	Yes	-	Yes	-	Yes	Yes	Definite
Schoenkerman and Lundstrom, USA (2009) [16]	M	59	-	-	Yes	-	Yes	-	Yes	-	-	-	Possible
Lim et al. Singapore (2011) [17]	M	69	Massive pus was found but no culture was mentioned	-	Yes	-	Yes	-	Yes	-	Yes	Yes	Possible
Furtado et al. India (2011) [18]	M	62	Yes	-	Yes	-	Yes	-	Yes	-	Yes	Yes	Definite
Patel et al. USA (2013) [19]	M	60	-	-	-	-	History of MRSA bacteremia	-	-	-	Yes	Yes	Possible
Morris et al. UK (2013) [20]	Fm	ND	-	-	Yes	-	Yes	-	Yes	-	Yes	Yes	Possible
Wedekind et al. Germany (2013) [21]	M	80	Purulent pericardial fluid	-	Yes	-	Yes	-	Yes	-	Yes	Yes	Possible
Chang et al. Taiwan (2014) [22]	M	38	Yes	-	-	-	Several times but unspecified	-	Yes	-	Yes	Yes	Definite
Satish et al. India (2015) [23]	ND	51	Yes	-	Yes	-	-	-	Yes	-	Yes	-	Definite
Roubelakis et al. UK (2015) [24]	M	62	Yes	-	-	-	-	-	Yes	-	Yes	Yes	Definite
Sekhar et al. India (2015) [25]	M	60	Yes	-	Yes	-	-	-	Yes	-	Complete occlusion of RCA (CTA)	Yes	Definite
Zateyshchikov et al. Russia (2015) [26]	M	45	-	Yes	Yes	-	-	-	-	-	Yes	-	Definite
Madkaiker et al. India (2016) [27]	M	50	Yes	-	Yes	-	-	-	Yes	-	-	-	Definite
Aggarwal et al. India (2016) [28]	M	51	Yes	-	-	-	-	-	Yes	-	Yes	Yes	Definite
Dalal et al. India (2017) [29]	Fm	66	Yes	-	Yes	-	-	-	Yes	-	Yes	-	Definite
Elder et al. Australia (2017) [30]	M	50	No specified data regarding 'infected stent'	-	Yes	-	Yes	-	Yes	-	Occluded LCx	Yes	Definite
Sangolkar et al. India (2018) [31]	M	66	No growth	-	-	-	-	-	Yes	-	Yes	Yes	Possible
Shetty et al. India (2018) [32]	M	52	Yes	-	-	-	-	-	Yes	-	Yes	Yes	Definite
Shah et al. India (2018) [33]	M	53	Yes	-	-	-	-	-	Yes	-	Yes	Yes	Definite
Sudhakar, India (2018) [34]	M	49	No growth	-	Yes	-	-	-	Yes	-	-	-	Possible
Messaoud et al. Tunisia (2019) [35]	M	71	-	-	Yes	-	-	-	Yes	-	Yes	Yes	Possible
Reddy et al. India (2019) [36]	M	50	Yes	-	Yes	-	Yes	-	Yes	-	Low-grade	Yes	Definite
Saeed et al. Qatar (2020) [37]	M	52	Yes	-	Yes	-	-	-	Yes	-	Yes	Yes	Definite
Saeed et al. Qatar (2020) [37]	M	50	No growth	-	-	-	-	-	Yes	-	Yes	Yes	Possible

Three or more of these following conditions are favorable for possible CSI: (1) coronary stent implantation in 4 weeks before; (2) repeated procedure through same vascular sheath or complications at the puncture site; (3) bacteremia; (4) fever above 101.5 F without any bacterial infection focus; (5) leukocytosis without any infection or acute coronary syndrome; (6) acute coronary syndrome; (7) cardiac imaging supports the presence of persistent inflammation.

Table 3 Antibiotics and surgical procedure

Author	Antibiotics	Administered Antibiotics	Antibiotics Duration	Surgery	Surgical Procedure
Leroy <i>et al.</i> France (1996) [6]	Yes	Ciprofloxacin, Amoxicillin-Clavulanate (1st tx)	2 weeks (1st tx) 3 weeks (2nd tx)	Yes	Infected stent removal, Debridement infected tissue
Bouchart <i>et al.</i> France (1997) [7]	Yes	IV Ciprofloxacin, Netilmicin (2nd tx)	3 weeks (3rd tx)	Yes	Infected stent removal, CABG
Grewe <i>et al.</i> Germany (1999) [8]	No	Ceftazidime-Amikacin-Ciprofloxacin, Imipenem	4 weeks	No	-
Liu <i>et al.</i> USA (2003) [9]	Yes	Ceftazidime-Amikacin	-	Yes	Infected stent removal, Debridement, CABG
Hoffman <i>et al.</i> Israel (2005) [10]	Yes	IV Naftcilin (1st tx)	20 days (1st tx)	No	-
Alfonso <i>et al.</i> Spain (2005) [11]	Yes	IV Naftcilin + Rifampicin (2nd tx)	7 weeks (2nd tx)	No	-
Marcu <i>et al.</i> USA (2005) [12]	Yes	IV Cloxacillin	6 weeks	Yes	Infected stent removal, CABG
Singh <i>et al.</i> India (2005) [13]	Yes	Oral Cloxacillin (1 st tx)	1 week (1st tx)	No	-
Garg <i>et al.</i> USA (2007) [14]	Yes	IV Cloxacillin + Gentamycin (2nd tx)	2 days (2nd tx)	Yes	Infected stent removal, CABG
Kishida <i>et al.</i> Japan (2007) [15]	Yes	IV Cefazoline	6 weeks	Yes	CABG
Schoenkerman and Lundstrom, USA (2009) [16]	Yes	Cloxacillin, Gentamicin	4 weeks	No	-
Lim <i>et al.</i> Singapore (2011) [17]	Yes	IV Vancomycin, Oral Rifampicin	>12 Days	Yes	Infected stent removal, Aneurysmal excision, Right ventricular wall reconstruction
Furtado <i>et al.</i> India (2011) [18]	Yes	Intravenous adapted antibiotics	>20 days	No	-
Patel <i>et al.</i> USA (2013) [19]	Yes	No Data	No data	Yes	Infected stent removal, Debridement, CABG
Morris <i>et al.</i> UK (2013) [20]	Yes	IV Vancomycin, IV Linezolid	No data	Yes	Infected stent removal, Debridement, CABG, Pus drainage
Wedekind <i>et al.</i> Germany (2013) [21]	Yes	Imipenem, Levofloxacin (1st tx)	1 week (1st tx)	Yes	Infected stent removal, Debridement, CABG
Chang <i>et al.</i> Taiwan (2014) [22]	No	IV Vancomycin, Oral Rifampicin (1st tx)	6 weeks (2nd tx)	Yes	Complete aneurysm excision, CABG
Satish <i>et al.</i> India (2015) [23]	Yes	IV Vancomycin, Oral Rifampicin (2nd tx)	6 weeks (1st tx)	No	-
Roubelakis <i>et al.</i> UK (2015) [24]	Yes	IV Vancomycin, Oral Rifampicin (2nd tx)	6 weeks (2nd tx)	No	-
Sekhar <i>et al.</i> India (2015) [25]	Yes	IV Vancomycin, Gentamycin	No data	Yes	Infected stent removal, CABG
Zateyshchikov <i>et al.</i> Russia (2015) [26]	No	Piperacillin/ Tazobactam, Clarithromycin (1st tx)	10 days (1st tx)	No	-
Madkaiker <i>et al.</i> India (2016) [27]	Yes	Cefuroxime, Ciprofloxacin	12 months (2nd tx)	Yes	Infected stent removal, CABG
Aggarwal <i>et al.</i> India (2016) [28]	Yes	Broad-spectrum antibiotics	No data	Yes	Infected stent removal, Aneurysm removal, CABG
Datal <i>et al.</i> India (2017) [29]	Yes	IV Flucloraxillin	6 weeks	Yes	Infected stent removal, Infected tissue resection, CABG
Elder <i>et al.</i> Australia (2017) [30]	Yes	No Data	3 weeks	Yes	Infected stent removal, Abscess removal, CABG
Sangolkar <i>et al.</i> India (2018) [31]	Yes	Inj. Meropenem, Teicoplanin	No data	Yes	Infected stent removal, Pus drainage, Debridement, CABG
Shetty <i>et al.</i> India (2018) [32]	Yes	IV Meropenem, IV Amikacin, IV Cefepime	8 weeks	Yes	CABG, Coronary pseudoaneurysmectomy, Necrotic tissue excision,
Shah <i>et al.</i> India (2018) [33]	Yes	IV Ceftazidime, IV Vancomycin, IV Gentamycin*	10 days (1st tx)	Yes	Infected stent removal, CABG
Sudhakar, India (2018) [34]	Yes	IV Ceftazidime, IV Vancomycin, IV Gentamycin*	6 weeks	Yes	Infected stent removal, Aneurysmal removal
Messaoud <i>et al.</i> Tunisia (2019) [35]	Yes	IV Ceftriaxone (1st tx)	*2 weeks due to ototoxicity	Yes	Infected stent removal, Aneurysmal removal
Reddy <i>et al.</i> India (2019) [36]	Yes	IV Ceftriaxone (2nd tx)	1 day (1st tx)	Yes	Infected stent removal, CABG
Saeed <i>et al.</i> Qatar (2020) [37]	Yes	Oral Ritiampicin and Fusidic Acid (3rd tx)	6 weeks (2nd tx)	Yes	Infected stent removal, Debridement
	Yes	IV Cefepime, Ciprofloxacin, Gentamycin	Indefinitely	Yes	Infected stent removal, Debridement, CABG
	Yes	No data	2 weeks	Yes	Infected stent removal, Aneurysm removal, Debridement, CABG
	Yes	No data	4 weeks	Yes	Infected stent removal, Aneurysm removal, Debridement, CABG
	Yes	IV piperacillin/tazobactam	No data	Yes	Infected stent removal, Mitral valve replacement, Debridement, CABG
	Yes	IV Meropenem, IV Gentamycin*, IV Ciprofloxacin	5 days (switched) 6 weeks	Yes	Infected stent removal, Debridement, CABG
	Yes	IV Vancomycin, IV Gentamycin, Oral Rifampicin	*2 weeks then switched to Ciprofloxacin	No	-
	Yes	No data	6 weeks	No	-
	Yes	IV Teicoplanin	4 weeks	Yes	Infected stent removal, CABG
	Yes	IV Piperacillin-Tazobactam, Vancomycin (1st tx)	5 days (switched)	Yes	Infected stent removal
	Yes	Penicillin G (2nd tx)	No data (2nd tx)	Yes	Infected stent removal, CABG
	Yes	IV Ceftriaxone (3rd tx)	6 weeks (3rd tx)	Yes	Infected stent removal, CABG
	Yes	Oral Amoxicillin (4th tx)	6 months (4th tx)	Yes	Infected stent removal, CABG

CABG, coronary artery bypass surgery; IV, intravenous; tx: therapy.

The current systematic review demonstrated a mortality rate among CSI patients of 26.47%. This rate is remarkably lower than those reported in previous reviews. For instance, previous reviews of 23 and 17 CSI cases yielded mortality rates of 39 and 47%, respectively [5,39]. One review also revealed mortality rates among patients with stent infections in coronary and noncoronary arteries of 48 and 23% [40]. The current review excluded reports mentioning a history of hemodialysis or surgery to minimize infection source bias. Meanwhile, previous reviews included all CSI cases, which is the most likely reason for the higher mortality rates [41].

Benefits to further clinical practice

The increasing use of PCI procedures and DES implantations could increase the incidence of CSI. Therefore, an updated outlook of PCI-related infections, especially CSI, is urgently needed. This review provides updated evidence to improve the recognition and management of CSI cases.

CSI is the rarest complication related to PCI, and it is avoidable. Patient preparation, personnel and laboratory cleaning significantly minimize the risk of infection [5]. Consequently, conditions such as sterility inadequacy, repeated local site punctures (primarily in the groin area), balloon or catheter re-utilization without adequate sterilization, repeated wire manipulations and prolonged indwelling catheterization can increase the risk of stent infection [36].

Study limitations

The present review has several limitations. First, this review excluded cases reported before the 2000s because most of these were inaccessible. Second, this review focuses solely on CSI cases without a history of hemodialysis or surgery, and, hence, evidence regarding CSI under these conditions is limited. However, hemodialysis and surgery are considered significant infection sources, which may cause bias [42]. Finally, data regarding patients' risk factors (diabetes, hypertension or any chronic illness) were not extensively assessed, as such factors are rarely mentioned.

Conclusion

This systematic review provides an updated outlook on CSI cases – namely, regarding clinical presentations, diagnostic methods, stents and vessel pathology, causative pathogens, treatments, complications and outcomes. This review could improve the recognition and management of CSI cases.

Acknowledgements

I.G.R.S. helped with concept, idea, investigation, checking and revising the article. K.L. helped with conceptualization, idea, data screening and extracting, analysis, writing and editing the article. R.F.A. helped with data

screening and extracting, analysis, write and check the manuscript. E.P.B.M. helped extract data, write, check and edit the manuscript. All the authors have read and approved the final manuscript.

The datasets used and/or analyzed during the current review are available from the corresponding author on reasonable request.

Conflicts of interest

There are no conflicts of interest.

References

- 1 Khan MA, Hashim MJ, Mustafa H, Baniyas MY, Al Suwaidi SKBM, AlKatheeri R, et al. Global epidemiology of ischemic heart disease: results from the global burden of disease study. *Cureus*. 2020; **12**:e9349.
- 2 Canfield J, Totary-Jain H. 40 years of percutaneous coronary intervention: history and future directions. *J Pers Med* 2018; **8**:E33.
- 3 Lim MJ. *Complications of Percutaneous Coronary Interventions*. The Interventional Cardiac Catheterization Handbook. 4th edition. Elsevier Inc.; 2018. pp. 261–285.
- 4 Günther HU, Strupp G, Volmar J, von Korn H, Bonzel T, Stegmann T. [Coronary stent implantation: infection and abscess with fatal outcome]. *Z Kardiol* 1993; **82**:521–525.
- 5 Franco JJ, Abisse SS, Ruisi P, Abbott JD. Infectious complications of percutaneous cardiac procedures. *Interv Cardiol* 2014; **6**:445–452.
- 6 Leroy O, Martin E, Prat A, Decoulex E, Georges H, Guillely J, et al. Fatal infection of coronary stent implantation. *Cathet Cardiovasc Diagn* 1996; **39**:168–170.
- 7 Bouchart F, Dubar A, Bessou JP, Redonnet M, Berland J, Mouton-Schleifer D, et al. Pseudomonas aeruginosa coronary stent infection. *Ann Thorac Surg* 1997; **64**:1810–1813.
- 8 Grewe PH, Machraoui A, Deneke T, Müller KM. Suppurative pancarditis: a lethal complication of coronary stent implantation. *Heart* 1999; **81**:559.
- 9 Liu JC, Cziperle DJ, Kleinman B, Loeb H. Coronary abscess: a complication of stenting. *Catheter Cardiovasc Interv* 2003; **58**:69–71.
- 10 Hoffman M, Baruch R, Kaplan E, Mittelman M, Aviram G, Siegman-Igra Y. Coronary stent bacterial infection with multiple organ septic emboli. *Eur J Intern Med* 2005; **16**:123–125.
- 11 Alfonso F, Moreno R, Vergas J. Fatal infection after rapamycin eluting coronary stent implantation. *Heart* 2005; **91**:e51.
- 12 Marcu CB, Balf DV, Donohue TJ. Post-infectious pseudoaneurysm after coronary angioplasty using drug eluting stents. *Heart Lung Circ* 2005; **14**:85–86.
- 13 Singh H, Singh C, Aggarwal N, Dugal JS, Kumar A, Luthra M. Mycotic aneurysm of left anterior descending artery after sirolimus-eluting stent implantation: a case report. *Catheter Cardiovasc Interv* 2005; **65**:282–285.
- 14 Garg RK, Sear JE, Hockstad ES. Spontaneous coronary artery perforation secondary to a sirolimus-eluting stent infection. *J Invasive Cardiol* 2007.
- 15 Kishida K, Nakaoka H, Sumitsuji S, Nakatsuji H, Ihara M, Nojima Y, et al. Successful surgical treatment of an infected right coronary artery aneurysm-to-right ventricle fistula after sirolimus-eluting stent implantation. *Intern Med* 2007; **46**:865–871.
- 16 Schoenkerman AB, Lundstrom RJ. Coronary stent infections: a case series. *Catheter Cardiovasc Interv* 2009; **73**:74–76.
- 17 Lim CP, Ho KL, Tan TT, Wong AS, Tan JW, Chua YL, Su JW. Infected coronary artery pseudoaneurysm after repeated percutaneous coronary intervention. *Ann Thorac Surg* 2011; **91**:e17–e19.
- 18 Furtado AD, Bhat SP, Peer SM, Chikkatur R. Infected pseudoaneurysm involving a drug-eluting stent. *Interact Cardiovasc Thorac Surg* 2011; **12**:636–637.
- 19 Patel AJ, Mehta RM, Gandhi DB, Bossone E, Mehta RH. Coronary aneurysm and purulent pericardial effusion: old disease with an unusual cause. *Ann Thorac Surg* 2013; **95**:1791–1793.
- 20 Morris TC, Davies O, Bradlow WM, Jeffery K, Bowler IC. Endovascular stent-associated infection with *Staphylococcus lugdunensis*. *BMJ Case Rep* 2013; **2013**:bcr2012008357.
- 21 Wedekind H, Grossekkettler U, Matheja P, Kleine-Katthoer P. PET-CT imaging in the diagnosis of coronary stent infection. *J Nucl Cardiol* 2013; **20**:1184–1185.

- 22 Chang WT, Lee CH. Massive coronary aneurysm after multiple percutaneous interventions: an iatrogenic or unpreventable disaster? *JACC Cardiovasc Interv* 2014; **7**:104–105.
- 23 Satish L, Sanghvi S. Coronary artery pseudoaneurysm: a rare case of coronary stent infection. *Indian Heart J* 2015; **67**:S65.
- 24 Roubelakis A, Rawlins J, Baliulis G, Olsen S, Corbett S, Kaarne M, Curzen N. Coronary artery rupture caused by stent infection: a rare complication. *Circulation* 2015; **131**:1302–1303.
- 25 Sekhar S, Vupputuri A, Nair RC, Palaniswamy SS, Natarajan KU. Coronary stent infection successfully diagnosed using ¹⁸F-fluorodeoxyglucose positron emission tomography computed tomography. *Can J Cardiol* 2016; **32**:1575.e1–1575.e3.
- 26 Zateyshchikov D, Fattakhova E, Demchinsky V, Baklanova T, Serebruany V. Late silent stent abscess. *Cardiology* 2015; **132**:65–67.
- 27 Madkaiker A, Krishna N, Kumaraswamy N, Varma P. Infected pseudoaneurysm of the left anterior descending artery. *BMJ Case Rep* 2016; **2016**:bcr2016216708.
- 28 Aggarwal P, Saxena P, Bhan A. Successful management of a giant unruptured mycotic coronary artery aneurysm after coronary angioplasty. *Indian Heart J* 2016; **68**(Suppl 2):S44–S46.
- 29 Dalal JJ, Digraikar A, Hastak M, Mulay A, Lad V, Wani S. Coronary stent infection – a grave, avoidable complication. *IHJ Cardiovasc Case Rep* 2017; **1**:77–79.
- 30 Elder A, Ho KC, Allman KC, Lowe H, Amos D, Adams M. What is this image? 2017: image 2 result: coronary stent infection diagnosed by gallium scan. *J Nucl Cardiol* 2017; **24**:1512–1514.
- 31 Sangolkar R, Ketana VRR, Sastry BKS. Coronary artery stent infection presenting as coronary cameral fistula: a case report. *Eur Heart J Case Rep* 2018; **2**:ty067.
- 32 Shetty LH, Ashalatha B, Sreedhar K, Manjunath CN. Giant mycotic RCA aneurysm - a very rare complication of PCI. *IHJ Cardiovasc Case Rep* 2018; **2**:S78–S80.
- 33 Shah D, Chag M, Shah D, Naik D, Chandan A, Sheth C, *et al.* Late coronary stent infection: a difficult to diagnose rare complication after percutaneous coronary intervention. *Indian J Thorac Cardiovasc Surg* 2019; **35**:74–77.
- 34 Sudhakar BGK. Pseudomonas aeruginosa septicemia resulting in coronary stent infection and coronary artery aneurysm and acute infective endocarditis of mitral valve causing severe mitral regurgitation- a case report. *IHJ Cardiovasc Case Rep* 2018; **2**:191–195.
- 35 Ben Messaoud M, Bouchahda N, Mahjoub M, Hmida B, Dridi Z, Gamra H. Case report: coronary artery stent infection with mycotic aneurysm secondary to tricuspid valve infective endocarditis. *F1000Res* 2019; **8**:853.
- 36 Reddy K V C, Sanzgiri P, Thanki F, Suratkal V. Coronary stent infection: interesting cases with varied presentation. *J Cardiol Cases* 2019; **19**:5–8.
- 37 Saeed W, Adam M, Abdallah TA, Omrani AS. Percutaneous coronary intervention-associated Actinomyces oris. *IDCases* 2020; **22**:e00929.
- 38 Dieter RS. Coronary artery stent infection. *Clin Cardiol* 2000; **23**:808–810.
- 39 Elieson M, Mixon T, Carpenter J. Coronary stent infections: a case report and literature review. *Tex Heart Inst J* 2012; **39**:884–889.
- 40 Bosman WM, Borger van der Burg BL, Schuttevaer HM, Thoma S, Hedeman Joosten PP. Infections of intravascular bare metal stents: a case report and review of literature. *Eur J Vasc Endovasc Surg* 2014; **47**:87–99.
- 41 Restrepo CS, Gonzalez TV, Baxi A, Rojas CA. Infected (“Mycotic”) coronary artery aneurysm: systematic review. *J Cardiovasc Comput Tomogr* 2020; **14**:e99–e104.
- 42 Kumbar L, Yee J. Current concepts in hemodialysis vascular access infections. *Adv Chronic Kidney Dis* 2019; **26**:16–22.