Szpital św. Wojciecha w Gdańsku

ANALIZA PRZYCZYN JATROGENNEGO USZKODZENIA TĘTNIC WIEŃCOWYCH ORAZ AORTY U PACJENTÓW PODDAWANYCH PRZEZSKÓRNYM PROCEDUROM KARDIOLOGICZNYM

ANALYSIS OF CATHETER-INDUCED CORONARY AND AORTIC INJURIES IN PATIENTS UNDERGOING PERCUTANEOUS CARDIOLOGICAL PROCEDURES

Rozprawa doktorska

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Serdecznie dziękuję mojej żonie Ani
za cierpliwość, wyrozumiałość oraz nieustające wsparcie.

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1. Wprowadzenie

Rozprawa doktorska pt. „Analiza przyczyn jatrogennego uszkodzenia tętnic wieńcowych oraz aorty u pacjentów poddawanych przezskórnym procedurom kardiologicznym" powstała w oparciu o zbiór trzech powiązanych tematycznie artykułów opublikowanych w międzynarodowych czasopismach naukowych indeksowanych w bazie PubMed oraz znajdujących się na liście Journal Citation Reports.

1.1 Wykaz publikacji stanowiących rozprawę doktorską:

Tytuł publikacji	Punkty MNiSW	Impact Factor
1. Catheter-induced coronary artery and aortic dissections. A study of mechanisms, risk factors and propagation causes. Klaudel J, Glaza M, Klaudel B, Trenkner W, Pawłowski K, Szołkiewicz M. Cardiol J. 2022. doi: 10.5603/CJ.a2022.0050	100	3,487
2. Analysis of reported cases of left main coronary artery injury during catheter ablation: In search of a pattern. Klaudel J, Trenkner W, Glaza M, Miekus P. J Cardiovasc Electrophysiol. 2019;30(3):410-426. doi: 10.1111/jce.13833	100	2,424
3. Delayed presentation of left main coronary artery dissection due to catheter ablation in a patient with bicuspid aortic valve. Coincidence or manifestation of inherent vulnerability? Klaudel J, Glaza M, Kosmalska K, Szolkiewicz M. J Cardiol Cases. 2020;22(6):269-272. doi: 10.1016/j.jccase.2020.07.004 The official journal of the Japanese College of Cardiology	20	-
Podsumowanie punktów	220	5,911

1.2 Wystąpienia zjazdowe związane tematycznie z rozprawą doktorską

1) **Klaudel J.** (2017). Redo ablation with catheter-induced coronary artery injury and subsequent myocardial infarction. EuroPCR Course 2017, annual meeting of the European Association of Percutaneous Cardiovascular Interventions (EAPCI), Paris, France. https://www.pcronline.com/Cases-resources-images/Resources/Course-videos-slides/2017/Unusual-cause-of-MI

2. Wykaz używanych skrótów oraz słowa kluczowe

BAV – bicuspid aortic valve / dwupłatkowa zastawka aorty

CCI - Catheter Culpability Index / współczynnik odpowiedzialności cewnika

CICAAD – catheter-induced coronary artery and aortic dissections / rozwarstwienia tętnicy wieńcowej i aortalne spowodowane przez cewnik

LAD – the left anterior descending artery / gałąź przednia zstępująca (lewa)

LCx – the left circumflex artery / gałąź okalająca (lewa)

LMCA – the left main coronary artery / pień lewej tętnicy wieńcowej

RFA – radiofrequency ablation / ablacja prądem o częstotliwości radiowej

SCAD – spontaneous coronary artery dissection / samoistne rozwarstwienie tętnicy wieńcowej

Słowa kluczowe: powikłania jatrogenne, rozwarstwienie tętnicy wieńcowej, jatrogenne rozwarstwienie aorty, uraz wywołany cewnikiem, powikłania ablacji arytmii

Keywords: iatrogenic complications, coronary artery dissection, iatrogenic aortic dissection, catheter-induced injury, cardiac ablation complications

3.Wstęp

Jatrogenne uszkodzenia tętnic wieńcowych i aorty, spowodowane mechanicznym, hydraulicznym lub termicznym oddziaływaniem cewnika diagnostycznego/mapującego lub zabiegowego, należą do najgroźniejszych powikłań procedur z zakresu elektrofizjologii oraz kardiologii interwencyjnej. Częstość ich występowania w przypadku koronarografii i angioplastyki wynosi poniżej 1% dla dyssekcji tętnic wieńcowych oraz 0,02-0,06% dla urazów aorty [1-4]. W trakcie zabiegów ablacji arytmii jeszcze rzadziej dochodzi do uszkodzeń tętnic wieńcowych – odsetek powikłanych procedur to około 0,03-0,09% [5-6]. Nieodwracalny uraz odejścia tętnicy wieńcowej, prowadzący do jej ciasnego zwężenia lub zamknięcia, niesie ze sobą ryzyko poważnych następstw klinicznych, zagrażających zdrowiu i życiu pacjenta. Wynika to z objęcia niedokrwieniem dużych obszarów mięśnia serca oraz możliwości propagacji uszkodzenia w obrębie opuszki i aorty wstępującej ze wszystkimi tego potencjalnymi konsekwencjami, w tym np. tamponady czy okluzji tętnic odchodzących od łuku aorty. Statystyki dowodzą, że śmiertelność wewnątrzszpitalna spowodowana rozwarstwieniem tętnicy wieńcowej, będącym następstwem koronarografii i/lub angioplastyki, wynosi ~6%, zaś jeżeli uszkodzenie dotyczy pnia lewej tętnicy wieńcowej (ang. the left main coronary artery - LMCA), odsetek ten sięga 15% [1, 7].

Dotychczas opublikowane prace, dotyczące uszkodzeń tętnic wieńcowych i/lub aorty wywołanych przez cewnik wieńcowy, skupiały się przede wszystkim na ocenie częstości występowania, rokowaniu oraz sposobie postępowania [1-4, 8]. I chociaż dostępne są ważne analizy prezentujące system klasyfikacji jatrogennych urazów LMCA i aortalno-wieńcowych, brak jest badań, które podjęłyby próbę określenia przyczyn i mechanizmów jatrogennego rozwarstwienia, zaś czynniki predysponujące do tego typu powikłań, zjawiska prodromalne oraz przyczyny propagacji uszkodzenia nie zostały jak dotąd precyzyjnie zdefiniowane [9, 10]. Ich ustalenie pozwoliłoby na wprowadzenie okołozabiegowych działań

zapobiegawczych, zwłaszcza w przypadku identyfikacji grup pacjentów szczególnie narażonych na tego rodzaju powikłania. Jak dotąd nie analizowano również częstości występowania jatrogennych dyssekcji w zależności od doświadczenia operatora i ośrodka. Wcześniejsze badania zależności powikłań zabiegowych i śmiertelności związanej z wykonaniem zabiegu angioplastyki wieńcowej sugerowały jedynie, że wraz z rosnącym doświadczeniem ośrodka i operatora oba te wskaźniki maleją [11, 12].

Problemem dotychczasowych publikacji jest również fakt, iż ich autorzy analizowali dyssekcje tętnic wieńcowych, wyłączając z badanej grupy rozwarstwienia opuszki i aorty wstępującej. Niezależnie od dużo gorszego rokowania i odmiennego postępowania w przypadku uszkodzenia obejmującego aortę, rozwarstwienie tętnicy wieńcowej przebiegające ze wsteczną propagacją do opuszki stanowi nie tylko anatomiczne, ale i patofizjologiczne continuum. Należy także dostrzec, że dostępne prace ograniczały się często do wyselekcjonowanych podgrup pacjentów np. populacji poddawanej procedurze rekanalizacji przewlekłych okluzji wieńcowych, czy osób z rozwarstwieniem zatoki Valsalvy [13, 14]. Jednocześnie największe badania dotyczące jatrogennych dyssekcji, w tym rejestry rozwarstwień aorty, zawierają wszelkie rodzaje uszkodzeń, czyli w dużej mierze dyssekcje spowodowane przez prowadnik, stent czy pęknięcie balonu, co uniemożliwia analizę mechanizmów i czynników ryzyka swoistych dla urazu odcewnikowego [3, 4, 15].

Poważne uszkodzenie odejścia tętnicy wieńcowej wywołane przez cewniki stosowane podczas procedur elektrofizjologicznych jest szczególnie niebezpieczne. Wynika to z większej sztywności cewników ablacyjnych oraz ryzyka poparzenia tętnicy wskutek omyłkowej aplikacji prądu o częstotliwości radiowej w jej bezpośrednim sąsiedztwie lub w jej świetle. Ponadto, gdy do urazu tętnicy wieńcowej dochodzi w trakcie koronarografii lub angioplastyki, rozpoznanie oraz leczenie jest zazwyczaj natychmiastowe, tymczasem w przypadku ablacji różnicowanie dolegliwości związanych z samą procedurą, czy też jej

ewentualnymi powikłaniami, bywa utrudnione, zaś możliwość interwencji opóźniona. Trudności te sprawiają, że część uszkodzeń rozpoznawana jest dopiero w przypadku propagacji urazu lub przypadkowo podczas późniejszych badań diagnostycznych [16].

Uszkodzenia ujść tętnic wieńcowych w czasie ablacji nie były dotąd przedmiotem systematycznych badań. Brak jest obecnie krajowych rejestrów czy wieloośrodkowych analiz powikłań wieńcowych, które towarzyszą procedurom inwazyjnego leczenia arytmii. Wśród dostępnych publikacji zdawkowo wspomina o nich jedynie Południowoamerykański Rejestr Procedur Ablacji (Latin American Catheter Ablation Registry) z 2012 roku oraz Hiszpański Rejestr Ablacji Przezskórnej (Spanish Catheter Ablation Registry) stanowiący oficjalny raport Grupy Roboczej ds. elektrofizjologii i arytmii Hiszpańskiego Towarzystwa Kardiologicznego (Spanish Society of Cardiology Working Group on electrophysiology and arrhythmias) [17, 18]. Wyjątkiem jest tu jedynie opublikowana tuż po powstaniu niniejszej pracy analiza Pothineni *i wsp.* [16]. Wobec braku innych źródeł, również ona oparta została o kwerendę internetowych baz artykułów medycznych i obejmuje przypadki uszkodzenia zarówno lewej, jak i prawej tętnicy wieńcowej, oraz ich gałęzi. Co ciekawe, autorom udało się odnaleźć jedynie 7 opisów urazu LMCA podczas ablacji.

W prezentowanym poniżej zbiorze publikacji przedstawiono analizę urazów spowodowanych przez cewnik, stanowiących powikłanie procedur z zakresu kardiologii interwencyjnej oraz elektrofizjologii. Ponadto, przedstawiono hipotezę roboczą o możliwej korelacji między dwupłatkową zastawką aortalną i zwiększoną podatnością na jatrogenne rozwarstwienia tętnic wieńcowych. W niniejszym omówieniu uwzględniono najnowsze publikacje z badanego obszaru, w tym również prace niedostępne w chwili przygotowywania artykułów stanowiących korpus dysertacji.

4. Cele pracy

Publikacja 1

1. Analiza mechanizmów jatrogennych rozwarstwień tętnic epikardialnych i aorty wstępującej wywołanych przez cewniki wieńcowe.
2. Identyfikacja czynników predysponujących, zjawisk prodromalnych oraz najczęstszych przyczyn propagacji dyssekcji.
3. Ocena wpływu doświadczenia operatora i ośrodka na częstość występowania jatrogennego rozwarstwienia naczyń.
4. Identyfikacja najbardziej niebezpiecznych rodzajów cewników wieńcowych.

Publikacja 2

1. Analiza śmiertelności wewnątrzszpitalnej oraz przebiegu klinicznego ostrej fazy uszkodzenia pnia lewej tętnicy wieńcowej podczas ablacji.
2. Wyodrębnienie typowych mechanizmów uszkodzenia LMCA oraz określenie rodzaju procedur elektrofizjologicznych obarczonych największym ryzykiem powikłań tego typu.
3. Ocena skuteczności metod leczenia urazu LMCA spowodowanego przez cewnik podczas ablacji arytmii.

Publikacja 3

1. Analiza hipotezy o zwiększonej podatności pacjentów z dwupłatkową zastawką aortalną na jatrogenne uszkodzenia ujść tętnic wieńcowych.

5. Materiał i metody

Publikacja 1

Analizę jatrogennych uszkodzeń tętnic epikardialnych i/lub aorty, które wystąpiły podczas przezskórnych zabiegów diagnostycznych i rewaskularyzacyjnych przeprowadzono retrospektywnie na podstawie bazy blisko 80 tysięcy procedur wieńcowych wykonanych w Szpitalu św. Wojciecha w Gdańsku oraz Szpitalu św. Wincentego a Paulo w Gdyni w latach 2000-2020. Selekcja pacjentów, u których stwierdzono spowodowane cewnikiem rozwarstwienie, została oparta na gromadzonych prospektywnie rejestrach powikłań oraz dodatkowo uzupełniona kwerendą elektronicznych baz protokołów zabiegowych z zastosowaniem słów kluczowych. Po wyłonieniu grupy 96 pacjentów z jatrogennym rozwarstwieniem tętnic wieńcowych i/lub aorty, dokonano porównania jej charakterystyki z ogólną populacją pacjentów, u których wykonywano procedury wieńcowe. W celu wyodrębnienia typowych mechanizmów dyssekcji szczegółowej analizie poddano obrazy angiograficzne zarejestrowane na nośnikach elektronicznych, pochodzące z zabiegów, podczas których wystąpiło to powikłanie. Oceny dokonało dwóch doświadczonych, samodzielnych operatorów kardiologii inwazyjnej. W razie braku zgodności, zasięgano opinii trzeciego kardiologa interwencjonisty. Po przeglądzie 60 pierwszych przypadków wyodrębniono 3 typowe mechanizmy dyssekcji oraz zidentyfikowano liczne czynniki predysponujące oraz prodromalne. Ponadto, od czasu rozpoczęcia projektu w 2017 roku, operatorzy zobowiązani byli sporządzać dokładny raport trudności napotkanych podczas powikłanego zabiegu, z uwzględnieniem potencjalnych mechanizmów odpowiedzialnych za uszkodzenie. Na podstawie analizy obrazów oraz ww. raportów, czynniki predysponujące zdefiniowano jako niemodyfikowalne warunki anatomiczne, zarówno prawidłowe (np. odejście tętnicy wieńcowej typu kostur pastuszy), jak i patologiczne, lub w postaci anomalii (np. blaszka miażdżycowa w ostium, tętniak aorty wstępującej, arteria lusoria), obejmujące

drogę dostępu tętniczego lub odejście tętnicy wieńcowej, utrudniające wprowadzenie i/lub manipulację cewnikiem. Czynniki zwiastunowe oznaczały modyfikowalne warunki śródzabiegowe, takie jak oddechowa niestabilność cewnika, nadmierne ograniczenie obrazu przez przesłony, czy efekt akordeonowy, bezpośrednio poprzedzające wystąpienie dyssekcji.

Na potrzeby badania oznaczono też tzw. współczynnik odpowiedzialności cewnika (ang. Catheter Culpability Index – CCI) wg następującego wzoru:

$$CCI = n/N \times 1000$$

gdzie n = liczba dyssekcji wywołanych przez dany typ cewnika, zaś N = całkowita liczba procedur, w których posłużono się owym cewnikiem. W ten sam sposób obliczano aortalny współczynnik odpowiedzialności cewnika (AoCCI).

Publikacja 2

W ramach tego projektu badawczego przeprowadzono analizę uszkodzeń pnia lewej tętnicy wieńcowej u pacjentów poddanych zabiegowi ablacji arytmii. Badaniem objęto wszystkie dostępne doniesienia opublikowane w latach 1987-2018 w internetowych bazach MEDLINE/PubMed oraz innych bazach artykułów medycznych, w tym wyniki prób klinicznych, rejestry procedur elektrofizjologicznych, opisy przypadków, abstrakty oraz prezentacje zjazdowe. Szczególną uwagę poświęcono publikacjom dotyczącym powikłań ablacji w obrębie jamy lewej komory i płatków aortalnych. Dokładnie analizowano również zestawienia i opisy przypadków izolacji uszka lewego przedsionka, ablacji dróg dodatkowych oraz częstoskurczu przedsionkowego z ogniska w obrębie lewego przedsionka, a także procedury wymagające dostarczenia energii w drodze odpływu prawej komory lub tętnicy płucnej ze względu na bliskość pnia lewej tętnicy wieńcowej do tych struktur. Łącznie zidentyfikowano 26 poważnych uszkodzeń pnia lewej tętnicy wieńcowej i jego rozgałęzień, jak również 2 przypadki „podrażnienia" LMCA, które zaowocowało przejściowym

niedokrwieniem. Odnaleziono także 2 opisy uszkodzenia ostium prawej tętnicy wieńcowej w czasie ablacji. W badanej populacji analizowano miejsce i technikę ablacji, rodzaj leczonej arytmii, objawy kliniczne oraz rokowanie. Zdefiniowano najczęstsze mechanizmy uszkodzenia, jak również określono grupę procedur obarczonych największym ryzykiem tego typu powikłań. Wyniki przedstawiono w tabeli w celu umożliwienia bezpośrednich porównań oraz wykorzystania pracy przez przyszłych badaczy tematu. Publikację uzupełniono o przegląd proponowanych metod zapobiegania uszkodzeniom tętnic wieńcowych podczas procedur elektrofizjologicznych przeprowadzanych w ich sąsiedztwie lub wymagających przejścia cewnikiem w ich pobliżu.

Publikacja 3

W pracy trzeciej - kazuistycznej, w oparciu o przegląd najnowszego piśmiennictwa dotyczącego genetycznego podłoża oraz patofizjologii dwupłatkowej zastawki aorty, wysunięto hipotezę o możliwej zwiększonej podatności pacjentów z tą wadą na zarówno samoistne, jak i jatrogenne rozwarstwienie ujść tętnic wieńcowych. Na kanwie przypadku klinicznego opisującego uszkodzenie pnia lewej tętnicy wieńcowej w trakcie przejścia cewnikiem ablacyjnym przez zastawkę aortalną, przedstawiono możliwe przyczyny większego zagrożenia jatrogennym urazem w tej grupie chorych.

5.1 Analiza statystyczna

W publikacji nr 1 przeprowadzono analizę porównawczą badanych populacji. Zmienne kategoryczne przedstawiono jako liczby oraz odsetki, i porównano przy pomocy analizy statystycznej z użyciem dokładnego testu Fishera. Zmienne ciągłe wyrażono jako wartości średnie ± odchylenie standardowe. Po potwierdzeniu jednorodności wariancji w badanych podgrupach za pomocą testu Levene'a, porównano je z wykorzystaniem testu t Studenta. Ze względu na dużą różnicę liczebności badanych grup, wyniki przeprowadzonych analiz

zweryfikowano testem U Manna-Whitney'a. Analiza statystyczna danych w publikacji nr 2 obejmowała obliczenia liczebności podgrup oraz udziału procentowego. Do analizy statystycznej zastosowano oprogramowanie Microsoft Excel oraz SPSS (IBM Corporation).

6. Podsumowanie wyników i wnioski

Zbiór prac stanowiących podstawę dysertacji pozwala określić najczęstsze mechanizmy wywołanego przez cewnik uszkodzenia ujść tętnic wieńcowych i/lub aorty, będącego jednym z najgroźniejszych powikłań inwazyjnych procedur wieńcowych i elektrofizjologicznych.

6.1 Publikacja 1

W pierwszym artykule oryginalnym wchodzącym w skład niniejszej rozprawy doktorskiej przedstawiono wyniki retrospektywnej analizy elektronicznych baz danych dwu pracowni kardiologii inwazyjnej, zawierających protokoły 76.104 inwazyjnych procedur wieńcowych wykonanych w latach 2000-2020. Zidentyfikowano łącznie 96 przypadków rozwarstwienia tętnic wieńcowych i/lub aorty wstępującej (ang. Catheter-Induced Coronary Artery and Aortic Dissection - CICAAD). Ogólna częstość występowania CICAAD wyniosła 0.126% oraz 0,021% w przypadku rozwarstwień obejmujących aortę. Śmiertelność wewnątrzszpitalna wyniosła 4,2% oraz 6,25% dla rozwarstwień aorty. U 15.6% pacjentów z CICAAD wystąpiła ostra niewydolność krążenia, przy czym u 10,4% była ona bezpośrednio związana z wystąpieniem dyssekcji.

Wyróżniono 3 podstawowe mechanizmy rozwarstwienia: śródścienne podanie kontrastu w wyniku klinowania się cewnika, traumatyczną intubację tętnicy wieńcowej lub jej reintubację w wyniku dyslokacji cewnika (wystąpiła ona u 28% pacjentów), oraz głębokie wprowadzenie cewnika w celu zwiększenia wsparcia lub jego niekontrolowane wciągnięcie do światła naczynia podczas usuwania balonów/stentów (obserwowane u 26% osób z

CICAAD). Zaklinowane wstrzyknięcie kontrastu było najczęstszym (46%) mechanizmem jatrogennego rozwarstwienia tętnicy wieńcowej, a także odpowiadało za wszystkie odcewnikowe rozwarstwienia aorty. U ponad połowy (52%) chorych z CICAAD zidentyfikowano co najmniej 1 czynnik predysponujący - najczęstszym z nich okazał się mały kaliber ujścia tętnicy wieńcowej i/lub zmiany miażdżycowe w jego obrębie (35%). Najczęściej stwierdzanymi zjawiskami prodromalnymi były: głęboka intubacja cewnika w celu uzyskania większego wsparcia (51%), nieosiowe położenie cewnika (34%) oraz wielokrotne uderzenie końcówki cewnika w ścianę naczynia (32%).

Częstość propagacji dyssekcji wyniosła 30,2% i spowodowała podwojenie liczby okluzji tętnic wieńcowych oraz rozwarstwień aorty. Warto zauważyć, że progresja rozwarstwienia do opuszki oraz dalszej części aorty wstępującej występowała szczególnie często (aż w 62,5% przypadków propagacji aortalnej), gdy śródścienne wstrzyknięcie kontrastu i spiralne rozwarstwienie tętnicy wieńcowej zostały zablokowane przez: obecność przewlekłej okluzji, krytycznego, zwapniałego zwężenia, wcześniej implantowany stent lub rozprężony balon. Najczęstszymi czynnikami wywołującymi narastanie rozwarstwienia były ponawiane podania kontrastu (62%) oraz kontynuowanie zabiegu przy użyciu tego samego cewnika (48%).

W porównaniu z populacją osób bez powikłań, wśród pacjentów z CICAAD częściej notowano płeć żeńską (48% vs. 34%, p=0.004), a także częściej występowały choroby towarzyszące: nadciśnienie tętnicze (56% vs. 25%, p<0.001), przewlekła choroba nerek (10% vs. 4%, p=0.002), ~~czy~~ ostry zawał serca (72% vs. 43%, p<0.001). Dyssekcja wystąpiła częściej podczas angioplastyki wieńcowej (85% vs. 39%, p<0.001) oraz w trakcie procedur z zastosowaniem dostępu od tętnicy promieniowej (77% vs. 65%, p=0.011).

Operatorzy wykonujący dużo procedur wieńcowych (>100 PCI) w roku poprzedzającym zdarzenie byli odpowiedzialni za 94% dyssekcji. W przypadku 84% powikłanych zabiegów, doświadczenie operatora w zakresie kardiologii interwencyjnej wynosiło ≥ 5 lat. Aż 98% jatrogennych rozwarstwień obserwowanych podczas angioplastyki wieńcowej było spowodowanych przez interwencjonistów wykonujących duże ilości procedur. W ciągu 21 lat objętych badaniem, CCIAAD występowało rocznie w 0-3 przypadkach na 1000 zabiegów, zaś roczny odsetek jatrogennych rozwarstwień uległ w badanym okresie zwiększeniu.

Do najgroźniejszych cewników, jeśli chodzi o liczbę spowodowanych dyssekcji, tj. o najwyższej wartości Catheter Culpability Index, należały: Hockey Stick, AllRight i Ikari Left. Stosunkowo bezpiecznymi krzywiznami okazały się cewniki Judkins Left, Judkins Right oraz Extra Backup. Cewnik Amplatz Left, mimo relatywnie niskiej wartości CCI, był jednakże odpowiedzialny za połowę przypadków jatrogennego urazu aorty.

Podsumowując, wywołane przez cewnik rozwarstwienia wieńcowe i/lub aortalne, jedynie w niewielkim odsetku wystąpiły u pacjentów bez czynników predysponujących (w postaci niekorzystnych warunków anatomicznych) i/lub bez zjawisk zwiastunowych (w formie przede wszystkim niebezpiecznego zachowania cewnika). Jatrogenne dyssekcje odcewnikowe najczęściej miały miejsce w trakcie pilnych interwencji wieńcowych wykonywanych u chorych wysokiego ryzyka przez doświadczonych operatorów. Najczęstszym, a zarazem najgroźniejszym mechanizmem dyssekcji – odpowiadającym za większość dyssekcji spiralnych (74%) oraz ostrych okluzji (67%), a także za wszystkie pierwotne i wtórne rozwarstwienia aorty – był uraz hydrauliczny, spowodowany zaklinowanym wstrzyknięciem kontrastu do ściany naczynia. U blisko 1/3 pacjentów doszło do propagacji dyssekcji, zaś roczny odsetek jatrogennych rozwarstwień nie uległ zmniejszeniu, mimo rosnącego doświadczenia ośrodka i operatorów.

W podgrupie pacjentów z nagromadzeniem czynników ryzyka CICAAD należy rozważyć użycie cewnika o mniej agresywnej krzywiźnie, a także zmianę dostępu na udowy, jeżeli podczas zabiegu od tętnicy promieniowej obserwuje się dużą niestabilność cewnika, lub też gdy kręty przebieg naczyń w śródpiersiu uniemożliwia jego kontrolę.

6.2 Publikacja 2

W drugiej publikacji wchodzącej w skład niniejszej rozprawy doktorskiej przedstawiono wyniki analizy jatrogennych uszkodzeń pnia lewej tętnicy wieńcowej, występujących w trakcie zabiegu ablacji arytmii. Analizie statystycznej poddano 22 przypadki urazu LMCA pochodzące z okresu 1993-2018. Ponadto zidentyfikowano 4 opisy selektywnego urazu gałęzi przedniej zstępującej i gałęzi okalającej spowodowane głęboką penetracją cewnika ablacyjnego w obrębie LMCA, a także 2 przypadki uszkodzenia ostium prawej tętnicy wieńcowej.

Całkowity odsetek zgonów (dla grupy 22 uszkodzeń LMCA) osiągnął wartość 27%. W grupie 19 poważnych urazów pnia lewej tętnicy wieńcowej z ostrym lub podostrymi objawami śmiertelność wewnątrzszpitalna wyniosła 32%. Wśród pacjentów leczonych w latach 1993-1997 odsetek zgonów sięgał 50%, natomiast w grupie 12 osób, u których uszkodzenie LMCA miało miejsce podczas ablacji w latach 2008-2018, wystąpił jedynie 1 śmiertelny przypadek. W grupie pacjentów z urazem rozpoznanym śródzabiegowo lub tuż po zabiegu, dla 14 osób dostępne były dokładne dane kliniczne. Wśród nich, sześciu pacjentów doznało wstrząsu kardiogennego lub głębokiej hipotonii wymagającej wlewu amin presyjnych lub wprowadzenia balonu do kontrpulsacji wewnątrzaortalnej, zaś u 7 osób wystąpiło migotanie komór, niestabilny hemodynamicznie częstoskurcz komorowy, burza elektryczna i/lub zatrzymanie krążenia. Ogółem, w 86% przypadków uszkodzenie LMCA przebiegało w sposób dramatyczny, wymagając defibrylacji, resuscytacji i/lub intubacji. Jedynie u 2 chorych z zachowanym przepływem w obrębie pnia lewej tętnicy wieńcowej

przebieg był średniociężki. U 55% pacjentów objawy wystąpiły do 30 minut po zabiegu, zaś odsetek podostrych przypadków (12-24h) wynosił 23%. U 14% pacjentów (3/22) obserwowano opóźnione wystąpienie objawów - w okresie od 2 miesięcy do 2 lat. Czas wewnątrzszpitalnego wystąpienia objawów nie korelował z przeżyciem, tzn. opóźnione ich wystąpienie w badanej grupie nie pogarszało rokowania. Wśród 4 pacjentów zmarłych w szpitalu z ostrą manifestacją objawów, u tylko jednego wystąpiły one w czasie zabiegu. U pozostałych trzech pogorszenie samopoczucia obserwowano w około 15-60 minut po zakończeniu ablacji, czyli po opuszczeniu sali zabiegowej.

Najczęściej stosowanym określeniem uszkodzenia stwierdzonego w koronarografii było „rozwarstwienie" i „skrzeplina". Spośród 22 pacjentów z uszkodzeniem LMCA, u 14 (64%) stwierdzono jednoznacznie, lub też wysunięto silne podejrzenie bezpośredniego urazu mechanicznego w wyniku penetracji pnia lewej tętnicy wieńcowej przez cewnik ablacyjny. U dwóch pacjentów z tej grupy w obrębie LMCA dokonano aplikacji energii podczas ablacji prądem o częstotliwości radiowej (ang. radiofrequency ablation – RFA). Wśród pozostałych 8 chorych, pięciu (23%) doznało urazu termicznego w trakcie RFA w wyniku aplikacji energii w pobliżu LMCA, u 1 osoby podejrzewano incydent zakrzepowo-zatorowy z następową okluzją LMCA, zaś w 2 przypadkach nie określono mechanizmu uszkodzenia. U 4 pacjentów z selektywnym urazem gałęzi LAD bądź też LCx (bez towarzyszącego uszkodzenia LMCA), jako przyczynę wskazano przypadkową penetrację naczynia przez cewnik ablacyjny.

Spośród wszystkich analizowanych przypadków uszkodzeń LMCA, aż osiemnaście (82%) wydarzyło się w trakcie ablacji w obrębie lewej komory lub jej drogi odpływu, i tym samym wymagało przejścia cewnikiem przez zastawkę aortalną. Jeśli uwzględnić selektywne uszkodzenia gałęzi LMCA (wszystkie 4 wydarzyły się podczas ablacji w obrębie lewej komory), odsetek ten jest jeszcze wyższy – 85%. Kolejne trzy procedury wykonywane były w obrębie płatków zastawki aortalnej, zaś jedna obejmowała ablację migotania przedsionków.

Wszystkie 22 procedury odbyły się pod kontrolą fluoroskopii. W przypadku 3 ablacji w obrębie lewej zatoki Valsalvy, przed zabiegiem wykonano koronarografię, nie stosowano natomiast echokardiografii wewnątrzsercowej.

W przypadku większości pacjentów (82%) uszkodzenie pnia lewej tętnicy wieńcowej zostało zidentyfikowane dopiero po wystąpieniu zmian w EKG i/lub ciężkich objawów niedokrwienia, zaś operator nie był świadomy przypadkowej penetracji naczynia, przemieszczenia cewnika i/lub wykonania aplikacji w pobliżu bądź w obrębie LMCA. Jedynie u 4 pacjentów udało się szybko rozpoznać nieprawidłową pozycję cewnika, z czego u dwóch doszło do jego przemieszczenia z jamy lewej komory lub jej drogi odpływu do opuszki aorty podczas aplikacji energii. Z owej dwójki, tylko u jednego chorego uszkodzenie LMCA zostało natychmiast rozpoznane, gdyż wystąpiło u niego zatrzymanie krążenia. U pozostałych dwóch pacjentów zauważono penetrację LMCA w trakcie próby sforsowania zastawki aortalnej, jednak zabieg był kontynuowany do czasu pojawienia się ciężkich objawów urazu naczynia.

Wśród 19 pacjentów, u których objawy uszkodzenia LMCA wystąpiły w trakcie pierwotnej hospitalizacji, dla 16 dostępne były dane odnośnie zastosowanego leczenia. Wszyscy pacjenci, których leczono metodą angioplastyki (75%), przeżyli zabieg, jednak u dwóch z nich był on powikłany: u 1 chorego po 3 godzinach doszło do progresji dyssekcji w kierunku gałęzi okalającej, zaś w drugim przypadku śródzabiegowo obserwowano wysunięcie się stentu ze skoagulowanego podczas ablacji pnia lewej tętnicy wieńcowej. Dwie osoby zostały poddane pilnemu zabiegowi pomostowania aortalno-wieńcowego i obie zmarły. U kolejnych dwóch pacjentów podjęto decyzję o dalszym postępowaniu zachowawczym – obaj wymagali rehospitalizacji w okresie 3 miesięcy od pierwotnego zabiegu. W przypadku pierwszym z powodu ostrego zawału serca powikłanego wstrząsem kardiogennym (leczony

stentowaniem LMCA), zaś w przypadku drugim, z powodu powiększającego się tętniaka LMCA (leczony operacyjnie).

Uszkodzenie LMCA należy do rzadkich powikłań zabiegu ablacji, jego przebieg jest zwykle dramatyczny i obarczony dużą śmiertelnością. Powikłanie to wymaga natychmiastowej diagnostycznej koronarografii i ratunkowej angioplastyki, która w badanej serii przypadków okazała się najskuteczniejszą metodą leczenia. Na podstawie analizowanego zbioru pacjentów można wnioskować, że do urazu pnia lewej tętnicy wieńcowej częściej może dochodzić w trakcie przechodzenia cewnikiem przez zastawkę aortalną, niż podczas wykonywania aplikacji w jego bezpośredniej okolicy, co zwykle wiąże się z zachowaniem większej ostrożności, poprzez np. mapowanie i oznaczania pozycji ostium LMCA. Mimo położenia LMCA w bliskim sąsiedztwie pnia tętnicy płucnej, przedniej ściany lewego przedsionka, podstawy uszka lewego przedsionka i wysokiej przegrodowej powierzchni drogi odpływu prawej komory, jak dotąd nie opisano przypadku uszkodzenia pnia lewej tętnicy wieńcowej podczas zabiegów ablacji wykonywanych w obrębie owych struktur. Jednym z najważniejszych ustaleń prezentowanej analizy był również bardzo duży - sięgający 82% - odsetek urazów LMCA niezauważonych przez operatora do czasu wystąpienia objawów. Wysoce niepokojące wydaje się także stwierdzenie możliwości podostrego (12-24h) lub bardzo późnego (2 miesiące – 2 lata) wystąpienia objawów uszkodzenia pnia lewej tętnicy wieńcowej, wymagające przedłużonego monitorowania oraz zwiększonej czujności diagnostycznej u pacjentów z wywiadem przebytej ablacji arytmii, zgłaszających dławicę lub inne objawy niedokrwienia sierdzia.

Od czasu publikacji artykułu (tj. od stycznia 2019 roku) ukazały się 3 kolejne raporty opisujące uszkodzenie LMCA w czasie ablacji komorowych zaburzeń rytmu [19-21]. W dwóch spośród nich uraz LMCA skutkował wystąpieniem wstrząsu kardiogennego i aktywności elektrycznej bez tętna, bądź też częstoskurczu komorowego wymagającego

kardiowersji. Dwaj pacjenci leczeni byli za pomocą ratunkowej angioplastyki wieńcowej i wymagali przedłużonego pobytu na oddziale intensywnej opieki medycznej. W trzecim przypadku podczas zabiegu wystąpiły zmiany niedokrwienne w EKG, zaś w pilnej koronarografii z użyciem ultrasonografii wewnątrznaczyniowej stwierdzono skurcz i obrzęk LMCA. U tego chorego zastosowano leczenie zachowawcze i ostatecznie rozpoznano okołozabiegowy zawał bez uniesienia odcinka ST. Dwa przypadki dotyczyły RFA w obrębie lewej zatoki Valsalvy, zaś jeden obejmował aplikacje prądu o częstotliwości radiowej w obrębie ciągłości mitro-aortalnej. W 2 przypadkach (1 ablacja w lewej zatoce Valsalvy i 1 ablacja w lewej komorze) pierwotnie nie rozpoznano przemieszczenia się cewnika do LMCA. U pacjenta z RFA w obrębie lewej komory post hoc stwierdzono, iż cewnik musiał uszkodzić pień lewej tętnicy wieńcowej podczas przechodzenia przez zastawkę aortalną. Wszyscy pacjenci przeżyli zabieg.

Publikacje te potwierdzają ustalenia niniejszej analizy odnośnie typu procedur elektrofizjologicznych obarczonych największym ryzykiem urazu LMCA, jego przebiegu klinicznego i najskuteczniejszego sposobu leczenia, a także mechanizmów uszkodzenia i opóźnionego rozpoznania dyslokacji cewnika. Mogą one również świadczyć (podobnie jak obserwacje analizy przedstawionej powyżej) o dużo lepszym obecnie rokowaniu pacjentów, będącym najpewniej konsekwencją ciągłego doskonalenia sprzętu i metody, a także powszechnej dostępności pracowni kardiologii inwazyjnej w ośrodkach wykonujących procedury elektrofizjologiczne.

6.3 Publikacja 3

W publikacji trzeciej - kazuistycznej, wchodzącej w skład rozprawy doktorskiej, przedstawiono przypadek uszkodzenia pnia lewej tętnicy wieńcowej podczas zabiegu ablacji drogi dodatkowej w obrębie lewej komory. Opisany pacjent został przyjęty trzy dni później z objawami zawału serca powikłanego wstrząsem kardiogennym. W ultrasonografii

wewnątrznaczyniowej uwidoczniono rozwarstwienie pnia lewej tętnicy wieńcowej w kierunku gałęzi LAD. Analiza zabiegu wskazywała na uraz LMCA spowodowany jego przypadkową penetracją podczas przejścia cewnikiem przez zastawkę aortalną. W artykule postawiono hipotezę o wyższym ryzyku jatrogennych uszkodzeń odejść tętnic wieńcowych u pacjentów z dwupłatkową zastawką aortalną (ang. bicuspid aortic valve – BAV) w związku ze wspólnym embriologicznym pochodzeniem tych struktur.

Wraz z wrodzonymi chorobami tkanki łącznej, takimi jak zespół Marfana, czy zespół Ehlersa-Danlosa, BAV zaliczana jest obecnie do grupy genetycznie uwarunkowanych schorzeń, przebiegających z zajęciem aorty (poszerzenie, tętniaki, rozwarstwienie, koarktacja) oraz arteriopatiami towarzyszącymi [20]. W przypadku BAV, poza aortopatią, opisywano m.in. zwiększoną częstość występowania tętniaków naczyń śródczaszkowych oraz samoistnych rozwarstwień tętnic szyjnych i wewnątrzczaszkowych [21, 22]. Obraz histopatologiczny wycinków ściany aorty w przypadku zespołu Marfana i BAV ma wiele cech wspólnych, w tym przede wszystkim zwyrodnienie błony środkowej (ang. medial degeneration), z nasiloną apoptozą komórek mięśni gładkich związaną m.in. z deficytem bądź dysfunkcją fibryliny-1, a także utratą białek fibrylarnych wskutek zwiększonej aktywności enzymów proteolitycznych - metaloproteinaz macierzy [23]. Procesy osłabiające ścianę naczyń krwionośnych czynią ją w przypadku tętnic epikardialnych bardziej podatną na samoistne rozwarstwienie (ang. Spontaneous Coronary Artery Dissection – SCAD), które u części chorych nie jest schorzeniem izolowanym, lecz odzwierciedleniem złożonej predyspozycji genetycznej i/lub uogólnionej patologii naczyń [24-27]. Samoistne rozwarstwienie tętnicy wieńcowej opisywane było u pacjentów z dwupłatkową zastawką aortalną, BAV stwierdzano ponadto u krewnych pacjentów ze SCAD częściej niż w populacji ogólnej [27, 28]. Z tego względu dwupłatkowa zastawka aortalna, wraz m.in. z zespołem Marfana, została uwzględniona w zaleceniach Amerykańskiego Towarzystwa

Kardiologicznego odnośnie screeningu w kierunku chorób towarzyszących i/lub predysponujących u pacjentów ze SCAD [29].

Komórki grzebienia nerwowego (ang. neural crest cells - NCCs), których dysfunkcja w okresie zarodkowym uznawana jest za jeden z podstawowych czynników patogenetycznych najczęstszej postaci BAV (przebiegającej ze zrośnięciem obu płatków wieńcowych, występującej u ok. 75-79% chorych z BAV), bezpośrednio uczestniczą w rozwoju warstwy mięśniowej ujść tętnic wieńcowych [30]. Pełnią one również rolę regulacyjną w rozwoju ich dalszych odcinków i odpowiadają m.in. za występowanie anomalii, ektazji oraz przetok wieńcowych do jam serca. To właśnie stwierdzane u pacjentów z BAV nieprawidłowości budowy i składu tkanki łącznej ściany naczyń tętniczych mogą być przyczyną obserwowanego u nich większego ryzyka SCAD [31]. Jednocześnie, jak wiadomo m.in. z badań Prakasha *i wsp.*, pacjenci z samoistną dyssekcją tętnicy wieńcowej, wskutek częstego współwystępowania u nich wrodzonych lub nabytych arteriopatii, są wielokrotnie bardziej narażeni na jatrogenne rozwarstwienie wieńcowe (opisywano także przypadki jatrogennej, wstecznej propagacji SCAD do aorty) [32-34]. Tym samym można przypuszczać, że u chorych z BAV również istnieje taka predyspozycja, tym bardziej, że w ich przypadku manipulacja cewnikami w obrębie opuszki aorty jest utrudniona przez jej zmienioną geometrię, zaś przejście przez nią dodatkowo utrudnia zrośnięcie płatków. Co więcej, u osób z BAV opisywano zwiększoną częstość występowania rzadkich wariantów i anomalii odejść tętnic wieńcowych, utrudniających podczas zabiegu ich lokalizację i/lub intubację, w tym tzw. wysokiego odejścia LMCA, tzn. lokalizacji ostium na poziomie lub powyżej połączenia zatokowo-cylindrycznego (ang. sinotubular junction), czy tzw. krótki pień lewej tętnicy wieńcowej (<5mm), lub też jego brak, z bezpośrednim odejściem gałęzi LMCA od zatoki Valsalvy [35-37]. Ostium LMCA i prawej tętnicy wieńcowej często przylega bezpośrednio do nieprawidłowo ukształtowanych spoideł zastawki aortalnej, co

może nakierowywać końcówkę zagiętego cewnika w stronę ujścia wieńcowego. Cewnik bowiem u pacjentów z BAV, w celu przejścia przez zastawkę musi ustawić się równolegle do spoideł, jest więc zwłaszcza u osób z przednio-tylną orientacją płatków (u których oba odejścia tętnic wieńcowych znajdują się w obrębie jednej zatoki wieńcowej powstałej ze zrośnięcia płatka prawo- i lewowieńcowego) naturalnie zwrócony w kierunku jednego z ujść wieńcowych. Na ryzyko związane z taką lokalizacją odejść tętnic wieńcowych zwracają uwagę „Wytyczne Amerykańskiego Stowarzyszenia Chirurgii Klatki Piersiowej dotyczące aortopatii związanej z dwupłatkową zastawką aortalną" (ang. „The American Association for Thoracic Surgery consensus guidelines on bicuspid aortic valve–related aortopathy" 2018) [38]. Manipulacja cewnikami w obrębie opuszki może być u pacjentów z BAV dodatkowo utrudniona przez jej poszerzenie, obejmujące często również dalszy odcinek aorty wstępującej, wynikające zarówno z postępu zaburzeń hemodynamicznych towarzyszących rozwijającemu się zwężeniu dwupłatkowej zastawki, jak i z wrodzonego defektu budowy ściany aorty. Wszystkie wyżej wymienione czynniki powodują, że kontrola cewnika jest u pacjentów z BAV szczególnie trudna, zaś penetracja LMCA lub jego gałęzi przez cewnik może zostać przeoczona (w przypadku jego nietypowego, np. wysokiego odejścia) i wyjątkowo głęboka, a zatem zwiększająca ryzyko poważnego urazu (w przypadku krótkiego pnia lub rozdzielnego odejścia LAD i LCx od opuszki).

Uwzględniając fakt, iż dwupłatkowa zastawka aortalna to najczęściej występująca wrodzona wada serca (0,5-2%), populacja pacjentów o potencjalnie większym narażeniu na jatrogenne rozwarstwienie ostium tętnicy wieńcowej, mogących wymagać ponadstandardowych środków ostrożności podczas procedur interwencyjnych oraz elektrofizjologicznych, jest zatem stosunkowo duża.

7. Streszczenie pracy w języku angielskim / Summary of the doctoral dissertation

Article 1

Catheter-induced coronary artery dissection is an infrequent but potentially life-threatening complication of percutaneous procedures. So far, only incidence, management, and prognosis of catheter-induced coronary artery and aortic dissections have been systematically studied. We sought to evaluate their mechanisms, risk factors, and propagation causes.

Electronic databases containing 76,104 procedures and complication registries from 2000-2020 were searched and relevant cineangiographic studies adjudicated. 96 dissections were identified. The overall incidence was 0.126%, and 0.021% for aortic injuries. In-hospital mortality rate was 4.2%, and 6.25% for aortic dissections. Compared to the non-complicated population, patients with dissection were more often female (48% vs. 34%, p=0.004), with a higher prevalence of comorbidities such as hypertension (56% vs. 25%, p<0.001) or chronic kidney disease (10% vs. 4%, p=0.002). They more frequently presented with acute myocardial infarction (72% vs. 43%, p<0.001), underwent PCI (85% vs. 39%, p<0.001), and were examined with a radial approach (77% vs. 65%, p=0.011). The most prevalent predisposing factor was small ostium diameter and/or atheroma. Deep intubation for support, catheter malalignment, vessel prodding were the most frequent precipitating factors. Of the three dissection mechanisms, ‘wedged contrast injection’ was the commonest (the exclusive mechanism of aortic dissections). Propagation rate was 30.2% and led to doubling of coronary occlusions and aortic extensions. The most frequent progression triggers were repeat injections and unchanged catheter. In 94% of cases, dissections were inflicted by high-volume operators, with ≥ 5-year experience in 84% of procedures. The annual dissection rate increased over 21-year timespan.

Catheter-induced dissection rarely came unheralded and typically occurred during urgent interventions performed in high-risk patients by experienced operators. The significant number of serious propagations underscores how many severe complications could potentially be avoided. Deeper understanding of the mechanisms and risk factors of catheter-induced dissections may help their prevention and enable prompt recognition and management.

Article 2

Left main coronary artery injury is a rare but potentially fatal complication of catheter ablation. Due to LMCA large perfusion area, its occlusion is usually a dramatic event. Reports of LMCA injury complicating catheter ablations from 1987 to 2018 were searched in electronic databases available online. Overall, 22 cases of serious LMCA damage have been identified. Additionally, 4 reports of direct mechanical trauma involving major LMCA branches induced by inadvertent catheter insertion have been studied. Typically (86%), LMCA injury presented as an acute/subacute complication of retrograde ablation in the left ventricle or the left ventricular outflow tract or aortic cusps. In at least 86% of patients with in-hospital presentation, LMCA trauma manifested dramatically as life-threatening arrhythmia, cardiogenic shock or severe hypotension requiring vasopressors. In-hospital mortality rate was 32%. Direct stenting has been found to be the most successful strategy.

One of the most important findings of this review is the significant number of non-acute cases (no less than 8 out of 22, i.e. 37%), and the high percentage of patients in whom LMCA injury initially went unnoticed (only in 4 cases , i.e. 18%, catheter dislodgement or its improper position was immediately recognized). A serious injury of LMCA or a major coronary branch with a significant flow compromise is unlikely to be asymptomatic. Delayed occlusions in some of the analyzed cases confirm the concern that in some patients the progression of coronary obstruction may be protracted. Despite the close proximity to the

pulmonary artery, the anterior left atrium, the base of the left atrial appendage, and high-septal right ventricular outflow tract, LMCA injury has not been reported for ablation targeting these structures. Ablation-related trauma of LMCA somewhat surprisingly seems to be more often a "collateral damage" of just passing by the artery ostium than a consequence of energy application in its close proximity.

LMCA injury, even if initially asymptomatic with normal angiographic appearance, may cause delayed flow deterioration, requiring prolonged monitoring and extended follow-up. Special caution should be given to the prevention whereas survival depends on prompt detection and treatment.

Article 3

The author's third publication, making up the doctoral dissertation, is a case report discussing a possible link between bicuspid aortic valve and the increased risk of iatrogenic coronary dissection. Arteriopathy in BAV is not limited to the aorta, and thus BAV is now considered a heritable disorder of connective tissue, associated with medial degeneration. This is emphasized by the fact that aortopathy and arteriopathy in BAV affect the vessels which embryological development is related to neural crest cells, that also directly contribute to the formation of the ostial regions of the coronary vessels. Moreover, research suggests that BAV may be a predisposing factor for spontaneous coronary artery dissection. In recent studies of spontaneous dissections, more than 17-fold higher incidence of catheter-induced coronary dissection has been found, despite the former primarily affecting the mid-distal segments and the latter ostial-proximal areas. Therefore, BAV patients may be doubly predisposed to iatrogenic coronary dissection; firstly, by more difficult catheter manipulation in the aortic root with the distorted cusp geometry, and secondly, by the underlying vulnerability of coronary ostia. With BAV being the most prevalent congenital heart disease,

our observation should caution doctors performing electrophysiological procedures near coronary ostia or requiring the aortic valve crossing, as well as interventional cardiologists to take special safety measures in such patients so as to prevent potentially fatal complications.

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10. PUBLIKACJE WCHODZĄCE W SKŁAD ROZPRAWY DOKTORSKIEJ / MANUSCRIPTS INCLUDED IN THE DOTORAL DISSERTATION

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Catheter-induced coronary artery and aortic dissections. A study of the mechanisms, risk factors, and propagation causes

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Catheter-induced coronary artery and aortic dissections. A study of mechanisms, risk factors and propagation causes.

Running head:

Analysis of catheter-induced coronary dissections

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ABSTARCT

Background So far, only incidence, management, and prognosis of catheter-induced coronary artery and aortic dissections have been systematically studied. We sought to evaluate their mechanisms, risk factors, and propagation causes.

Methods Electronic databases containing 76,104 procedures and complication registries from 2000-2020 were searched and relevant cineangiographic studies adjudicated.

Results 96 dissections were identified. The overall incidence was 0.126%, and 0.021% for aortic injuries. In-hospital mortality rate was 4.2%, and 6.25% for aortic dissections. Compared to the non-complicated population, patients with dissection were more often female (48% vs. 34%, p=0.004), with a higher prevalence of comorbidities such as hypertension (56% vs. 25%, p<0.001) or chronic kidney disease (10% vs. 4%, p=0.002). They more frequently presented with acute myocardial infarction (72% vs. 43%, p<0.001), underwent PCI (85% vs. 39%, p<0.001), and were examined with a radial approach (77% vs. 65%, p=0.011).

The most prevalent predisposing factor was small ostium diameter and/or atheroma. Deep intubation for support, catheter malalignment, vessel prodding were the most frequent precipitating factors. Of the three dissection mechanisms, 'wedged contrast injection' was the commonest (the exclusive mechanism of aortic dissections). Propagation rate was 30.2% and led to doubling of coronary occlusions and aortic extensions. The most frequent progression triggers were repeat injections and unchanged catheter. In 94% of cases, dissections were inflicted by high-volume operators, with ≥5-year experience in 84% of procedures. The annual dissection rate increased over 21-year timespan.

Conclusions Catheter-induced dissection rarely came unheralded and typically occurred during urgent interventions performed in high-risk patients by experienced operators.

INTRODUCTION

Catheter-induced coronary artery dissection is an infrequent but potentially life-threatening complication of percutaneous procedures. We have recently studied its patterns in electrophysiological procedures; however, the incidence is much greater for coronary interventions (1, 2). Involving proximal segments of major coronary vessels, it usually jeopardises a large myocardial area, and may propagate into the aorta more easily than guidewire-related dissections. It is also more dangerous than injuries induced by a balloon or stent, as it may occur prior to coronary artery wiring or during diagnostic angiography.

Traditionally, studies of iatrogenic dissections focused on one dissected vessel or structure, be it the left main coronary artery (LMCA) or the sinus of Valsalva (SoV), thereby presenting only selective data (2-6). Still others exclusively included dissections complicating specific procedures, such as chronic total occlusion interventions (7). Registries of iatrogenic injuries of the aorta are also available, and though catheter-induced aortocoronary dissection is a distinct entity with its specific risks and treatment, coronary artery dissection and its retrograde extension into the aorta represent not only an anatomic but a pathophysiologic continuum as well (8). At the same time, various dissection-triggering devices (e.g. wires, stents) were usually taken into account, which precluded the analysis of mechanisms and factors specific to the catheter-related trauma. We sought to identify all catheter-induced injuries complicating coronary procedures to analyse the mechanisms of dissection, predisposing and precipitating factors, and propagation causes. Iatrogenic complications are avoidable by their nature, it is thus crucial to search for patterns and risk factors.

METHODS

We performed a retrospective study of catheter-induced coronary artery and aortic dissections (CICAAD) at two high-volume centres. CICAAD cases (including coronary graft dissections)

were retrieved from prospectively collected registries of procedural complications. They were double-checked by a query of electronic catheterization databases, utilizing keywords such as dissection, iatrogenic, spiral, or extraluminal. Recorded images of the right coronary artery (RCA) intervention with multiple stents as well as *ad hoc* angioplasty of LMCA were additionally reviewed to check for underreported cases. All CICAAD angiograms were assessed by two interventionists to confirm and classify a dissection, its mechanism, predisposing and precipitating factors, and propagation causes. If there was a discrepancy, a third reviewer was included in the adjudication.

Definitions

Dissections were graded according to the National Heart, Lung, and Blood Institute criteria, Eshtehardi and Dunning classification (Supplementary Table 1) (9, 10).

After the review of the first 60 cases, a consensus was reached to discern three main mechanisms of dissection. 'Wedged contrast injection' was defined as a primarily hydraulic injury caused by contrast agent delivery with damped outflow, i.e., catheter tip embedded in the artery wall. Initial vessel wall filling was usually recorded *in statu nascendi* with dye persistence afterwards. 'Forceful catheter engagement' (or vigorous pecking motion) described mechanical trauma caused by a catheter tip impact with a spot damage of a coronary artery or the aortic wall, typically inflicted at first contact with forceful intubation and immediately visible, or after vigorous pecking at a vessel wall. 'Deep catheter insertion' indicated a long-segment mechanical injury caused by deep intubation for support, or by inadvertent catheter dragging into a vessel during difficult device retrieval.

Multiple predisposing and precipitating factors suggestive of their role in the injury have been identified. They were assigned after cineangiography review. Since the project launch in 2017, operators provided internal reports detailing problems encountered during CICAAD

procedures, with presumable triggers pointed out. Predisposing factors were defined as unmodifiable anatomic conditions, both normal (e.g. shepherd's crook takeoff) and anomalous or pathological (e.g. arteria lusoria, ostial atheroma), involving the arterial access route or a coronary artery origin, making it difficult to advance and/or manipulate a catheter. Precipitating factors included modifiable conditions that could have been reversed or corrected, such as catheter behaviour (e.g. respiratory instability), vessel response (e.g. concertina effect), or procedural conditions (excessive blending).

Hemodynamic collapse was defined as new signs and symptoms of organ hypoperfusion with systolic blood pressure drop <90 mmHg, frequently requiring inotrope infusion and intra-aortic balloon pump insertion. Periprocedural infarction was defined according to the 2018 Fourth Universal Definition of Myocardial Infarction (11).

Low, medium and high-volume operators were defined as per ACCF/AHA/SCAI 2013 update of the competence statement on coronary interventions and the paper by Fanaroff *et al.* (12, 13). As complicated cases are usually taken over by senior interventionists, for the purpose of volume and experience estimation, the initial, culprit operator data was taken into account.

To account for each curve's dissection potential, Catheter Culpability Index (CCI) was calculated with a following formula (Aortic CCI was calculated in the same way):

$$CCI = n/N \times 1000,$$

where n=number of dissections induced by a particular curve, N=number of procedures in which the curve was used.

Statistical analysis

Categorical variables are presented as numbers and percentages, and compared with Fisher exact test. Continuous variables were checked for normal distribution and expressed as means

±standard deviation, with comparisons made using Student's t-test. Due to CICAAD vs. non-CICAAD cohorts' unequal sample size, the results were verified and confirmed with Mann-Whitney U test. P-values were two-sided with a significance level of 0.05. Analyses were performed using SPSS version 24.0 (IBM Corp., Armonk, NY).

RESULTS

CICAAD incidence

Overall, 76,104 diagnostic and therapeutic coronary procedures were performed between June 2000 and September 2020, and 96 cases of coronary artery (including 2 saphenous grafts) and aortic dissection were identified. The total incidence of CICAAD was 0.126%, with the aortic involvement in 0.021% (16 cases). During the 21-year timespan, dissection occurred annually in 0-3 cases per 1000 procedures (Figure 1). No dissection caused by sheathless and guide extension catheters was found.

CICAAD vs. non-CICAAD cohort

Compared to the non-CICAAD population, patients with dissection were significantly more often female (48% vs. 34%, p=0.004), with a higher prevalence of comorbidities such as hypertension (56% vs. 25%, p<0.001), chronic kidney disease (10% vs. 4%, p=0.002), and prior stroke (8.3% vs. 2.8%, p=0.006) (Table 1). They were more likely to present with acute myocardial infarction (72% vs. 43%, p<0.001), and undergo PCI (85% vs. 39%, p<0.001), with transradial access also more frequently utilised in this group (77% vs. 65%, p=0.011). Six French catheters were significantly more often used in the procedures complicated by dissection (81% vs. 44%, p=0.012), as opposed to five French, more commonly utilised in the non-CICAAD group (55% vs. 16%, p<0.001).

Dissection and procedure characteristics

The right and left coronary artery (LCA) were almost equally affected, in 47% vs. 46%, respectively (Table 2). The right sinus of Valsalva was dissected in twice as many cases as the left (8 vs. 4). The ascending aorta dissection extending above SoV occurred in 8 cases (8%), in 6 involving the right cusp.

Reassuringly, all dissections manifested acutely during index procedure, and no cases of urgent reintervention due to delayed occlusion caused by unrecognised or conservatively treated dissection were found. In 30%, dissection occurred during an off-hours procedure (Table 2). Automatic injection of contrast was used in 35% of all CICAAD, and in 46% of aortic dissections. Dissections were managed conservatively in 28%, with stent in 71%, and surgically in 2%.

Hemodynamic Collapse and Mortality

The in-hospital mortality rate for all dissections was 4.2%, and 6.25% for dissections involving the aorta. Four patients with CICAAD died during index hospitalization, and in 3 of them, death could be attributed to the consequences of dissection or its management.

In 15.6% of cases, hemodynamic compromise was observed (Table 2). Five patients were either admitted in shock or manifested circulatory instability due to slow flow during primary angioplasty, while in the remaining ten, the collapse could be attributed to the dissection. Of the ten dissection-related hemodynamic collapses (6 spiral RCA occlusions, 2 zipper and 1 spiral LMCA dissection, and 1 left anterior descending artery injury), in eight cases vessel occlusion occurred (with cardiac arrest in five). Eight of these patients had been admitted with acute coronary syndrome.

Predisposing and precipitating factors

In 52% of CICAAD, at least one predisposing factor has been identified (Table 3). Cases of unfavourable origin of a coronary artery were more often found than unfavourable arterial access route (49% vs 7%, respectively). Among the former, small proximal diameter and/or ostial atheroma were the most commonly identified (35%), whereas the most frequent access route obstacle was mediastinal arteries tortuosity.

The most commonly observed phenomena precipitating dissection were catheter deep seating or deep insertion during device delivery/removal (51%), catheter malalignment (34%), vessel prodding (32%), catheter systolic-diastolic mobility (27%), and respiratory instability (14%).

Mechanisms of dissection and its propagation

'Wedged contrast injection' proved to be the most common mechanism of CICAAD (46%) (Table 3). It was also responsible for all cases of primary aortic or aortocoronary dissection (11 patients). 'Forceful catheter engagement' and 'deep catheter insertion for device delivery/retrieval' were implicated in 28% and 26% of cases, respectively.

The overall propagation rate was as high as 30.2%. In 13,5% of CICAAD patients, the propagation was minor without flow impairment, while in the remaining 16.7%, it was serious, leading to spiral dissection, vessel occlusion, or retrograde extension into the aorta. The main causes of dissection expansion (multiple factors were often found in one patient) were repeat injections (62%), unchanged catheter (48%), and not immediately stenting a dissection (35%). Four out of eight aortic dissections extending above SoV occurred due to the progression of the original coronary artery injury. Main aortic propagation triggers (found in all such cases) were repeat injections and unchanged catheter. In 10 out of 16 aortic dissection cases, the retrograde propagation to the aorta was the consequence of downstream

expansion having been blocked by a stent, chronic total occlusion, or a tight and/or calcified lesion.

Individual and institutional expertise

Most dissections (94%) were caused by high-volume interventionists (>100 PCI/year), whose invasive experience in 84% of cases was at least 5 years (Figure 2A-B). Only in 6 cases, an operator had performed <100 PCI in the preceding 12 months and had <3 years of experience. Dissections during angioplasty were caused by high-volume operators in 98% of cases (Figure 2C).

Catheter Culpability Index

As per CCI, the most offending curves were HS III, ART4.5, IL3.5, and HS II (for catheter names see Table 4); however, being overall rarely used, they all caused only 6% of all dissections (Figure 3; Table 4). The lowest CCI values (<10) were calculated for EBU4.0, BLK4.0, Judkins Left and Right curves, with Judkins curves being the most commonly used. The highest Aortic CCI was calculated for HS II, AL1, and TIG4.0 curves, with AL1 implicated in 50% of aortic injuries.

DISCUSSION

Catheter-induced coronary and aortic dissections have not been systematically studied as far as mechanisms of injury and its propagation, risk factors, and operator's competence are concerned. There is only anecdotal evidence on triggers and predictors of catheter-related trauma, and even seminal papers by Dunning and Eshtehardi were based on small series of 9 and 28 patients, respectively (2, 9, 14).

Incidence

The largest so far study of catheter-induced coronary dissections reported 0.09% incidence and 5.9% mortality; findings similar to our population, with 80 isolated coronary injuries (0.105%) and 3.75% mortality (10). A retrospective analysis of complications of diagnostic cardiac catheterization found coronary dissection in 0.003% of patients, corresponding to 0.004% in our sample (3 diagnostic angiography-related dissections) (15). In the analyses of iatrogenic aortic dissections, triggers other than a catheter were also included, with the calculated catheter-induced injuries rate ranging from 0.017% to 0.067%, as compared to 0.021% in our material (4, 5). The cited mortality rate for the aortic dissections was 2.7%, and 6.25% in our cohort. Dunning *et al.* reported a 0.02% rate of iatrogenic aortocoronary injuries, which in our population amounted to 0.014% - 11 cases (9). In keeping with its reported vulnerability, the right SoV was dissected twice more often than the left, and the dissection propagated above the aortic root three times more often during RCA cannulation (5, 16). A novel finding of the study is that in 62.5% of aortic dissections, the retrograde extension into the aorta occurred when the downstream progression was blocked by a stent, chronic occlusion or a tight, calcified lesion. In the presence of such antegrade obstacles, catheter wedging is particularly dangerous, as intramural contrast injection is redirected into the aortic root wall.

CICAAD vs. non-CICAAD cohort

We did not find any significant differences between CICAAD and non-CICAAD populations regarding age and body mass index. Not unexpectedly for an adverse event cohort, CICAAD patients had more comorbidities and more often presented with acute myocardial infarction. As in previous reports, we also observed a much higher rate of dissections induced by guiding as compared to diagnostic catheters (85% vs. 15%, respectively, $p<0.001$), with the diagnostic catheter being responsible for only 1 out of 16 cases of the aortic involvement (2, 4, 5, 7, 10).

The relation between the access route and catheter-induced injury has not been evaluated so far, although two studies did observe a higher prevalence of transradial approach in procedures complicated by dissection. (10, 17).

Predisposing and precipitating factors

Several types of ominous situations and dangerous catheter behaviour portending dissection have been identified in the CICAAD cohort, suggesting that catheter-induced injuries rarely come unheralded. Many of them have been previously mentioned in case reports/series (2, 3, 14, 18). Despite all the disadvantages of a retrospective analysis, only in 48% of patients, no predisposing factors were found, and in just 14.6%, no precipitating factors were present, while in the rest, multiple triggers typically contributed to a dissection.

The data on the incidence of coronary artery origin variants in general population are not available in literature; however, with 14% and 13% rate, respectively, both the superior and inferior takeoffs are likely to be overrepresented in the CICAAD group. Although not considered as predisposing to dissection *per se*, they may impede coaxial catheter alignment and its stable positioning. Similarly, Shepherd's crook type of RCA origin (4.3%) and coronary artery ectopy rate (3.2%), with cited incidence for the latter of 0.05–0.1%, were relatively high in our cohort.

Mechanisms of dissection and its propagation

Wedged contrast injection appears to be the commonest and most dangerous dissection mechanism. It was implicated in 46% of coronary dissections, 75% of spiral dissections, and exclusively responsible for primary aortic injuries. Although not always the principal mechanism of injury, intentional or inadvertent deep catheter insertion was observed in nearly half of CICAAD, suggesting that deep penetration of the vessel may facilitate subsequent dissection by its wall disruption. The mechanisms identified in our analysis, though never

systematically studied before, are in concert with the observations of previous case series (2, 3, 14, 18).

Iatrogenic propagation rate of 30% is a disturbing finding, and though local expansion cases were also included, repeated injections or sticking to the culprit catheter led to doubling of occlusive dissections. Moreover, out of eight aortic dissections extending above SoV, four could have been avoided as they were caused by a retrograde progression. In a 2010 study of iatrogenic LMCA dissections, the reported propagation rate was also alarmingly high, reaching 32% (2).

Operator's and centre's expertise

Both individual and institutional learning curves have been described for coronary invasive procedures, and inverse relationship between operator's angioplasty volume and in-hospital mortality was reported (13). However, in the majority of the study cases, dissections were inflicted by high-volume operators with extensive experience. Despite equipment sophistication, the annual rate of dissections did not decrease with growing individual and institutional experience, showing an upward trend (Figure 1). This fact, however disappointing, may at least partially be explained by more complex procedures having been performed over time, with older and sicker patients qualified to intervention.

Catheter Culpability Index

The most harmful catheter curves are reported in our study not just in absolute numbers but in relation to their overall use. CCI was calculated to compensate for the fact that the most frequently utilised catheters typically cause more dissections (Figure 3). Non-conventional guides (e.g. HS or ART), are more challenging to handle and thus less commonly used, which accounts for an explosive combination of operator's low familiarity and catheter's high aggressiveness. Even with their infrequent usage, their CCI value was disproportionately

high. Uncommonly employed curves (<1% usage) accounted for 12% of dissections, although they comprised only 2.2% of all catheters used. Regular extra support guides like AL1 and EBU (both accounting for 14% of used catheters), despite their reported notoriety, had relatively low CCI, even though they were responsible for almost half of dissections (49%) (4, 9, 10). Amplatz Left, however, had the second-biggest Aortic CCI and was implicated in nearly half of aortic dissections (7/16), as also suggested by previous studies (4, 8). This correlation may be due to Amplatz's frequent usage in RCA interventions and RCA's susceptibility to retrograde dissection (16) (Figure 4). Equally surprising was a good track record of bilateral catheters, infamous for popping into coronary ostia and dissection potential (3, 18). On the other hand, despite being implicated in 37.5% of dissections, Judkins catheters had the lowest CCI thanks to their frequent utilization (73% of all used catheters).

Study limitations

Evaluation of uncommon complications is necessarily based on retrospective analyses. This is the largest series presented so far; however, 96 patients are too small a number to draw definite conclusions. Despite the relative uniformity of techniques, our study may not reflect practices and equipment used elsewhere. To limit the observer bias, all cases were reviewed by two operators, with a third interventionist called in whenever a discrepancy arose. Risk factors such as prohibitive chest vasculature, or radial artery spasm, were probably more prevalent than could be deduced *a posteriori*. As in any *post hoc* analysis, the causative role of the identified precipitating factors is speculative; however, they were repeatedly observed in the studied cohort and regularly preceded the injury.

CONCLUSIONS

It was the complexity and urgency of a procedure that decided the fate of a dissection rather than the operator's inexperience. The significant number of serious propagations underscores how many severe complications could potentially be avoided.

Deeper understanding of the mechanisms and risk factors of catheter-induced dissections may help their prevention and enable prompt recognition and management.

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CONFLICT OF INTEREST STATEMENT

The authors report no competing interests.

ABBREVIATIONS LIST

CCI - Catheter Culpability Index

CICAAD - catheter-induced coronary artery and aortic dissections

LCA – the left coronary artery

LMCA - the left main coronary artery

RCA - the right coronary artery

SoV - the sinus of Valsalva

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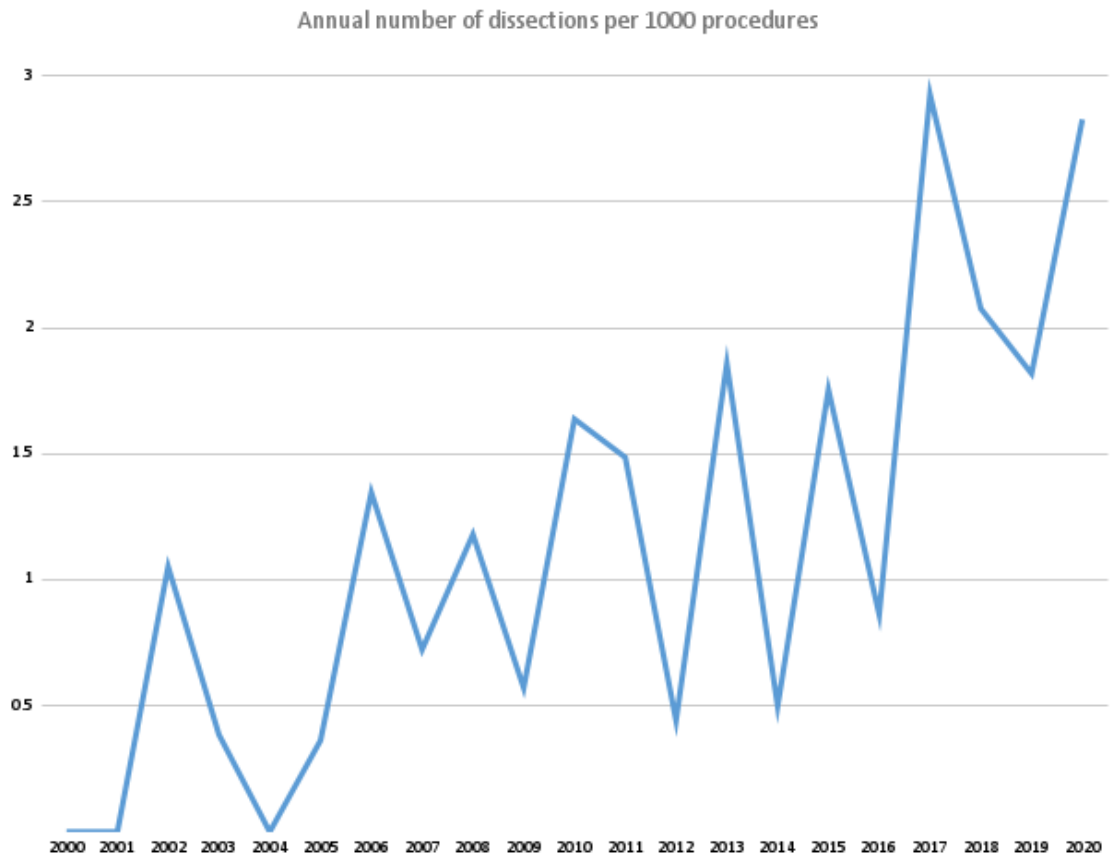

Figure 1 Annual number of catheter-induced coronary artery and aortic dissections per 1000 procedures.

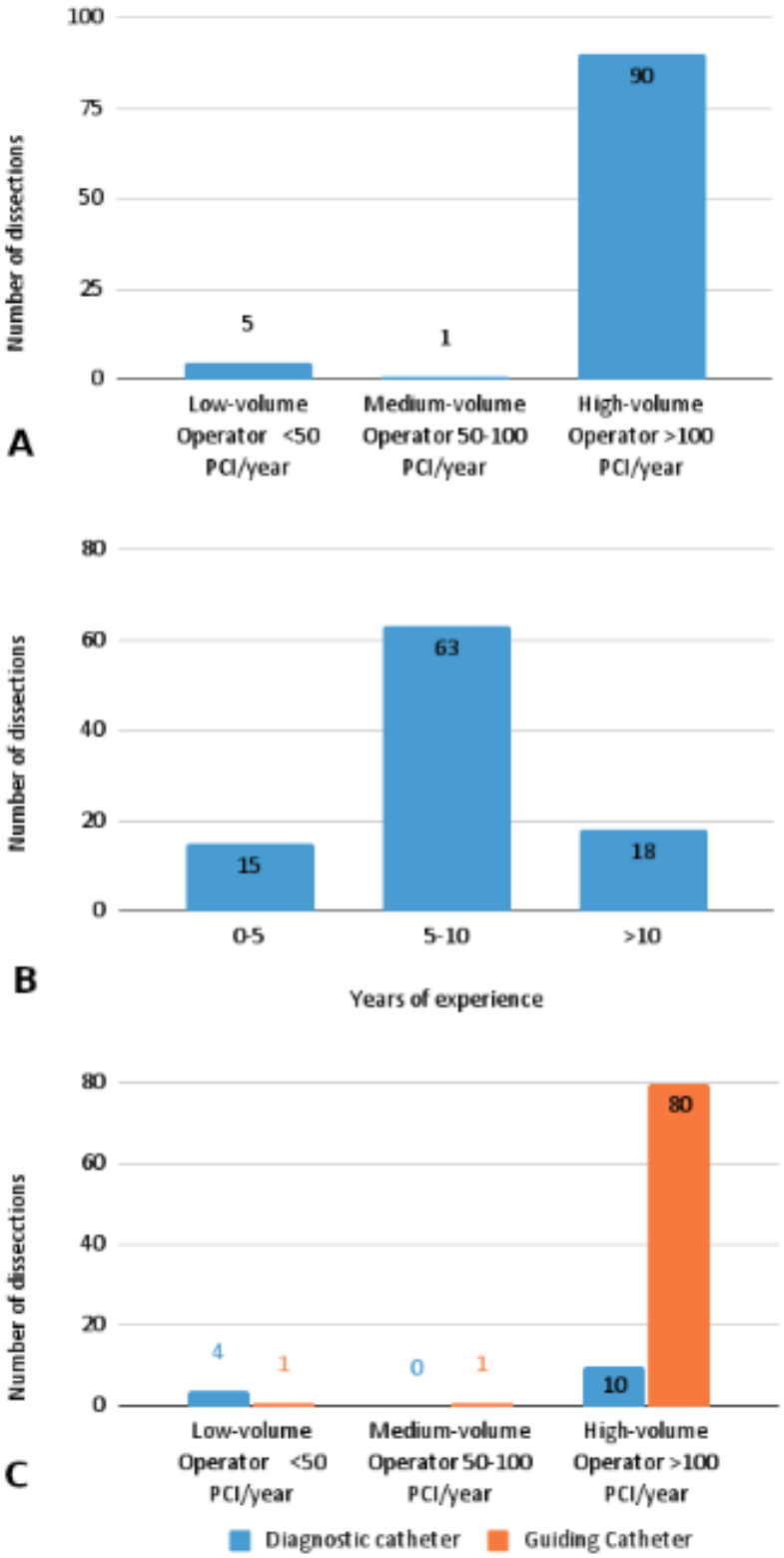

Figure 2 (A) Operator's PCI volume and (B) experience 12 months prior to dissection; (C) operator's PCI volume 12 months prior to dissection induced by a diagnostic vs. guiding catheter. PCI – percutaneous coronary intervention.

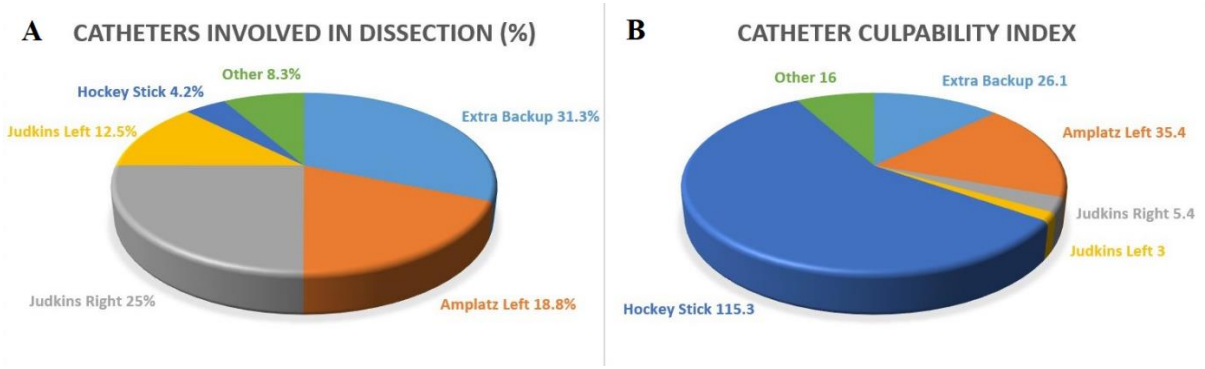

Figure 3 (A) Catheter curves involved in dissections (%); (B) Catheter Culpability Index as calculated for major catheter curves.

Table 1 Baseline characteristics

	Non-CICAAD n = 76008	**CICAAD n = 96**	**p value**
Age, years	65.5 (11.5)	67.8 (11.6)	0.061
Female	25619 (33.7)	46 (47.9)	0.004
Body mass index	27.9 (4.5)	27.5 (4.4)	0.399
Diabetes mellitus	11503 (15.1)	21 (21.9)	0.085
Hypertension	18759 (24.7)	54 (56.3)	<0.001
Chronic kidney disease	2719 (3.6)	10 (10.4)	0.002
Peripheral arterial disease	1417 (1.9)	5 (5.2)	0.034
Stroke	2119 (2.8)	8 (8.3)	0.006
COPD	1189 (1.6)	5 (5.2)	0.018
Prior myocardial infarction	15101 (19.9)	22 (22.9)	0.449
Prior PCI	15950 (20.9)	29 (30.2)	0.029
Prior CABG	4479 (5.9)	6 (6.3)	0.827
CCS/CHF/valvular disease/other	35282 (46.4)	24 (25.0)	<0.001
Acute coronary syndrome	40726 (53.6)	72 (75.0)	<0.001
Unstable angina	7876 (10.4)	3 (3.1)	0.017
Acute myocardial infarction	32850 (43.2)	69 (71.9)	<0.001
NSTEMI	12176 (16.0)	29 (30.2)	<0.001
STEMI	20674 (27.2)	40 (41.7)	0.002
Prehospital cardiac arrest	1103 (1.5)	4 (4.2)	0.052
Shock at admission	822 (1.1)	3 (3.1)	0.087
Femoral access	26615 (35.0)	22 (22.9)	0.015
Arm access (any arm artery)	49393 (65.0)	74 (77.1)	0.011
Diagnostic coronary angiography	46467 (61.1)	14 (14.6)	<0.001
PCI	29541 (38.9)	82 (85.4)	<0.001
CTO PCI	3104 (4.1)	7 (7.3)	0.117
Catheter size			
4 French	371 (0.3)	1 (1.0)	0.375
5 French	65498 (55.2)	15 (15.6)	<0.001
6 French	52451 (44.2)	78 (81.3)	0.012
7 French	247 (0.2)	2 (2.1)	0.040

Values are numbers (%) or means (SD). CABG – coronary artery bypass grafting; CCS - chronic coronary syndrome; CHF – congestive heart failure; CICAAD – catheter-induced coronary artery and aortic dissection; CTO - chronic total occlusion; NSTEMI - non–ST-segment elevation myocardial infarction; PCI - percutaneous coronary intervention; STEMI - ST-segment elevation myocardial infarction; COPD – chronic obstructive pulmonary disease.

Table 2 Characteristics of procedures complicated by catheter-induced dissection

Dissection characteristics

	n = 96
Dissected vessel:	
LMCA	32 (33.3)
LAD	6 (6.3)
LCX	6 (6.3)
AL	1 (1.0)
All LCA dissections	44 (45.8)
RCA	45 (46.9)
SVG	2 (2.1)
Aortic involvement:	16 (16.7)
Sinus of Valsalva	12 (12.5)
(Isolated SoV dissection)	5 (5.2)
Right SoV	8 (8.3)
Left SoV	4 (4.2)
Ascending aorta above SoV:	8 (8.3)
Inflicted during RCA cannulation	6 (6.3)
Inflicted during LCA cannulation	2 (2.1)
Aortic involvement due to antegrade coronary propagation blocked by stent, CTO, or tight/calcified lesion	10 (10.4)
Dissection NHLBI type:	
Localized A-B	36 (37.5)
Extensive C-F	55 (57.3)
LMCA dissection Eshtehardi type I	25 (26.0)
Type II	5 (5.2)
Type III	2 (2.1)
Aortic dissection Dunning type I	8 (8.3)
Type II	5 (5.2)
Type III	3 (3.2)

Procedural characteristics

Automatic contrast injection	34 (35.4)
Acute presentation of dissection	96 (100)
Dissection preceded by another complication (e.g. lost stent, broken wire)	8 (8.3)
Dissection followed by another intraprocedural complication (e.g. stent thrombosis)	5 (5.2)
Flow deterioration (by at least 1 TIMI grade)	24 (25.0)
Acute occlusion	18 (18.8)
Hemodynamic collapse due to dissection	10 (10.4)
Troponin rise indicative of periprocedural MI (or re-increase incute MI)	18 (18.8)
Off-hours catheterization/PCI	29 (30.2)

Management	
Conservative	27 (28.1)
Stenting (or balloon inflation)	68 (70.8)
Surgery	2 (2.1)
Operator's individual experience	
Cath lab practice, yrs	10.7 (5.5)
Mean procedures performed 12 months prior to CICAAD, n	750 (307)
Mean PCI performed 12 months prior to CICAAD, n	351 (168)
In-hospital adverse events	
Death	4 (4.2)
Death in aortic dissection	1 (1.0)
Stroke	2 (2.1)
Urgent target vessel revascularization due to thrombosis or dissection	3 (3.1)
Shock	12 (12.5)
CA/VF/CPR during procedure	7 (7.3)
Stent intraprocedural /acute/in-hospital thrombosis	3 (3.1)

Values are numbers (%) or means ± standard deviation. AL – anterolateral branch; CA - cardiac arrest; CICAAD – catheter-induced coronary artery and aortic dissection; CPR – cardiopulmonary resuscitation; CTO - chronic total occlusion; LAD – left anterior descending artery; LCA – left coronary artery; LCX – left circumflex artery; LMCA – left main coronary artery; MI – myocardial infarction; NHLBI – National Heart, Lung, and Blood Institute; PCI – percutaneous coronary intervention; RCA – right coronary artery; SoV – sinus of Valsalva; SVG – saphenous vein graft. TIMI – thrombolysis in myocardial infarction; VF – ventricular fibrillation.

Table 3 Risk factors and mechanism of dissection and its propagation

Predisposing factors:	**n = 49 (52.1)**
Unfavorable origin of coronary artery (n = 94, excluding SVG dissections n = 2), multiple choice:	46 (48.9)
Ostial-proximal atheroma and/or small ostial-proximal diameter (<3.0mm)	39 (41.5)
Ectopic coronary artery	3 (3.2)
Coronary ostium ectasia	2 (2.1)
Shepherd's crook	2 (4.3)
Unfavorable arterial access route (multiple factors in one patient not encountered):	7 (7.3)
Tortuosity of mediastinal arteries or low aortic origin of innominate artery	3 (3.1)
Dilated ascending aorta (aneurysm)	1 (1.0)
Arteria lusoria	1 (1.0)
Brachial loop	1 (1.0)
Difficult radial artery passage due to small diameter (or spasm)	1 (1.0)
Tortuous/stenosed iliac arteries	0
Abdominal aorta aneurysm	0
Precipitating factors (multiple choice):	**n = 82 (85.4)**
Catheter deep seating or deep insertion during device delivery/removal (>10mm)	49 (51.0)
Non-coaxial catheter alignment	33 (34.4)
Repeated vessel wall prodding with catheter tip	31 (32.3)
Catheter systolic-diastolic mobility (>5mm or dislodgement)	26 (27.1)
Too aggressive catheter	20 (20.8)
Too aggressive catheter – left coronary artery	16 (16.7)
Too aggressive catheter – right coronary artery	4 (4.2)
Catheter respiratory instability (>10mm or disengagement)	13 (13.5)
Excessive blending (catheter tip obscured)	11 (11.5)
Another complication preceding dissection (lost stent, broken wire, etc.)	7 (7.3)
Accordion effect	2 (2.1)
Coronary spasm	1 (1.0)
Mechanisms of dissection and its propagation	**n = 96**
Dissection mechanism (primary):	
Wedged contrast injection	44 (45.8)
Forceful catheter engagement (or vigorous pecking motion)	27 (28.1)
Deep catheter insertion (for device delivery or retrieval)	25 (26.0)
Aortocoronary dissection mechanism (aortic dissections secondary to propagation excluded):	n = 11
Wedged contrast injection	11 (100)
Propagation	**n = 29 (30.2)**
Propagation type:	
Minor	13 (12.5)
Vessel occlusion	9 (9.4)
Retrograde to SoV and SoV + the ascending aorta	5 (65.2)

Non-occlusive spiral dissection	2 (2.1)
Propagation causes (multiple choice):	
Repeated injections	18 (62.1)
Unchanged catheter (or its position)	14 (48.3)
Dissection not stented immediately or incompletely covered	10 (34.5)
Dissection unnoticed or misinterpreted	8 (27.6)
Catheter inserted through dissected segment	3 (10.3)
Excessive blending	2 (6.9)
False lumen wired or stented	2 (6.9)
Wire removal	1 (3.4)

Values are numbers (%). SoV – sinus of Valsalva; SVG – saphenous vein graft.

Table 4 Catheter Culpability Index (CCI) and Aortic Catheter Culpability Index (AoCCI)

Curve	% of all catheters used	n of dissections	CCI	n of aortic dissections	AoCCI
HS III	0,10	2	181,8	0	0
ART 4.5	0,06	1	156,3	0	0
IL 3.5	0,06	1	149,3	0	0
HS II	0,20	2	84,4	1	42,2
CLS 4.0	0,13	1	66,7	0	0
LCB	0,13	1	66,2	0	0
AL 1	4,39	18	35,4	8	15,7
EBU 3.75	5,38	21	33,8	2	3,2
JCL 3.5	0,34	1	25,1	0	0
EBU 3.5	2,77	8	25,0	1	3,1
Q 3.5	0,40	1	21,5	0	0
TIG 4.0	0,75	1	11,5	1	11,5
JL 3.5	8,98	6	5,8	0	0
JR 4.0	36,03	23	5,5	2	0,5
EBU 4.0	1,79	1	4,8	0	0
JR 3.5	2,40	1	3,6	0	0
BLK 4.0	2,45	1	3,5	0	0
JL 4.0	25,61	6	2,0	1	0,3
Catheter family					
Hockey Stick	0,30	4	115,3	1	28,8
Extra BackUp	9,93	30	26,1	3	2,6
Judkins Right	38,43	24	5,4	2	0,5
Judkins Left	34,60	12	3,0	1	0,3

Catheter name abbreviations: AL - Amplatz Left; ART – allRight; CLS - Contralateral Left Support; EB (or XB) - Extra Backup; HS - Hockey Stick; IL - Ikari Left; JCL - Judkins Curve Left; JL - Judkins Left; JR - Judkins Right; LCB - Left Coronary Bypass; Q - Q curve; TIG – Tiger.

CCI (Catheter Culpability Index) = number of CICAAD events induced by a given curve divided by number of procedures in which the curve was used, times 10,000. Aortic CCI (AoCCI) was calculated in the same way.

Supplementary Table 1 Dissection classifications

National Heart, Lung, and Blood Institute Coronary Artery Dissection Classification	
A	Luminal haziness or minor radiolucent areas within the lumen during contrast injection with no persistence after dye clearance or flow impairment
B	Parallel tracts or double lumen separated by a radiolucent area during contrast injection with minimal or no persistence after dye clearance, and without flow impairment
C	Extraluminal cap with persistence of contrast after dye clearance from the lumen
D	Spiral luminal filling defects, usually with excessive and persistent contrast staining of the false lumen, often with delayed antegrade flow ("barber shop pole")
E	New, persistent filling defects within the coronary lumen
F	Non A-E types that lead to impaired flow or total occlusion
Eshtehardi Left Main Coronary Artery Dissection Classification	
Type I	Localized dissection
Type II	Dissection with extension into major branches ("zipper")
Type III	Dissection with extension to aortic root
Dunning Classification of Coronary Dissection With Retrograde Extension Into The Aortic Root	
Class I	Involving the ipsilateral cusp
Class II	Involving cusp and extending up the aorta less than 40 mm
Class III	Involving cusp and extending up the aorta greater than 40 mm

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CLINICAL REVIEWS

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Analysis of reported cases of left main coronary artery injury during catheter ablation: In search of a pattern

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Abstract

Introduction: Left main coronary artery (LMCA) injury is a rare but potentially fatal complication of catheter ablation. Due to LMCA large perfusion area, its occlusion is usually a dramatic event.

Methods and Results: Reports of LMCA injury complicating catheter ablations from 1987 to 2018 were searched in electronic databases. Twenty-two cases of serious LMCA damage have been identified. Additionally, four reports of direct mechanical trauma involving major LMCA branches induced by inadvertent catheter insertion have been studied. Typically 86% LMCA injury presented as an acute/subacute complication of retrograde ablation in left ventricle/left ventricular outflow tract or aortic cusps. In at least 86% of patients with an in-hospital presentation, the LMCA trauma manifested dramatically as a life-threatening arrhythmia, cardiogenic shock, or severe hypotension requiring vasopressors. In-hospital mortality rate was 32%. Direct stenting has been found to be the most successful strategy.

Conclusion: LMCA injury, even if initially asymptomatic with normal angiographic appearance, may cause delayed flow deterioration, requiring prolonged monitoring and extended follow-up. Special caution should be given to the prevention whereas survival depends on prompt detection and treatment.

KEYWORDS

aortic cusp ablation, catheter ablation complication, left main coronary artery iatrogenic dissection, left main coronary artery injury, retrograde ablation

1 | INTRODUCTION

Efficacy and safety of catheter ablation are well-established. Serious complications are infrequent and rarely fatal. Coronary artery injury (CAI) is one of the potentially disastrous adverse events related to the procedure. In multicenter ablation registries of all types of arrhythmia, its incidence is below 1%. First large-scale surveys, such as NASPE (1995) and ATAKR (1999), indicated that CAI was almost exclusively limited to the endocardial ablation of accessory pathways (AP).[1,2] This was determined by the fact that the procedures are performed near the atrioventricular groove, that is, the region closest to the anatomical course of two major coronary arteries. Moreover, patients with Wolff-Parkinson-White syndrome constitute a significant percentage of all electrophysiological procedures. With the sophistication of ablation techniques, new areas were targeted in the 90s, including coronary sinus and aortic cusps. Development of standard anticoagulation protocols encouraged retrograde procedures with a growing number of the left ventricle (LV) and aortic root ablations. This boosted procedure success rate and opened a way both to new arrhythmic targets and new mechanisms of CAI. Nonetheless, in more contemporary studies, the incidence of CAI is low, namely, 0.03% to 0.09% for all ablations.[3,4] Specific types of procedures predispose to this particular complication, for example, a study of epicardial ablation of posteroseptal APs within coronary

venous system reported 15% of CAI.[5] Aortic cusp ablation is associated with energy delivery closest to coronary ostia, that is, with potentially the largest area of myocardium at risk of ischemia. In small case series and literature reviews, the reported incidence of CAI is 0%.[6–8] However, several reports of CAI associated with the aortic root ablation have been published.[9–13] Not all cases of CAI are apparent with symptoms and electrocardiographic changes; therefore, its actual incidence is likely to be underestimated and underreported. CAI rate is significantly higher in studies designed to detect it, or in high-risk procedures with routine angiography performed before and after ablation.[5]

Several mechanisms of CAI have been identified.[14] Transient, relievable spasm related to radiofrequency (RF) energy application has most often been described. Despite heparin administration and routine activated clotting time (ACT) testing, thromboembolic events have been observed for retrograde and transseptal procedures as no anticoagulation protocol completely abolishes char and thrombus formation. However, stroke and transient ischemic attack are most often reported. Case reports of coronary air embolism complicating transseptal ablation of atrial fibrillation have been published, too. Preferential migration of air bubbles into the right coronary artery (RCA) has been observed due to the most superior position of the vessel ostium in a supine patient. Another mechanism of CAI is direct mechanical trauma of coronary ostia, induced by an ablation catheter during retrograde procedures, with or without concomitant energy application.[15–17] This can lead to severe intimal disruption with thrombus formation or artery wall dissection with intramural hematoma and/or intraluminal clot.

When a major coronary artery is severely injured, the presentation is most often acute or subacute as symptomatic myocardial ischemia with chest pain, ventricular arrhythmia, conduction disturbances, and sometimes hemodynamic instability. If the injured artery is a relatively small vessel or the lumen is not totally occluded, CAI may manifest itself as a troponin rise with relievable chest discomfort, which in sedated patients may be attenuated and confused with typical ablation-related complaints. Increased troponin concentration is not a specific marker for CAI as the cardiac injury is often observed as a consequence of catheter ablation with troponin levels rising well into the range for diagnosis of myocardial infarction. Late presentations of CAI have also been described. In such patients, energy application or direct mechanical trauma gradually leads to progressive coronary artery stenosis or chronic total occlusion, which may become symptomatic only with time or be incidentally detected months or years postindex procedure.[9,10,18,19]

Left circumflex (Cx) and right coronary artery branches are the most commonly affected during ablation procedures as they amount to 75% of all CAI reports.[20] Owing to their anatomical course, LMCA and left anterior descending artery (LAD) are less frequently damaged. In the case of LMCA acute injury, the clinical presentation is usually dramatic due to the large area of myocardium at risk. Depending on the domination type (right coronary artery vs left vs balanced type), LMCA provides 54% to 100% of LV muscle perfusion.[21] Thus, spontaneous myocardial infarctions caused by LMCA occlusion or critical stenosis are commonly associated with cardiogenic shock and/or cardiac arrest. In a meta-analysis of LMCA angioplasty in spontaneous acute myocardial infarction published in 2012, 26% of patients presented with cardiogenic shock.[22]

In 2015, an urgent percutaneous angioplasty of LMCA was performed at our center in a young man with Wolff-Parkinson-White syndrome (Figure 1).[23] The patient had just undergone retrograde redo ablation of left AP at another hospital. Before the rescue stenting, LMCA dissection was established in intravascular ultrasound (IVUS) examination (Figure 2). Subsequent analysis of the case led us to search the literature for reports of ablation-related coronary artery lesions, with particular regard to LMCA injury.

2 | METHODS

A comprehensive search of relevant registries, clinical studies, case reports and case series, reference lists of related articles, abstracts, and oral presentations reporting ablation-related coronary artery injuries published in Medline/PubMed/electronic databases has been conducted. Special caution has been given to reports of adverse events complicating LV, the left ventricular outflow tract (LVOT) and aortic cusps ablation. Surveys and reports of left atrial appendage isolation and left atrium ablation in atrial fibrillation, focal atrial tachycardia, atrial insertions of APs, as well as procedures with energy delivery in the right ventricular outflow tract (RVOT), and the pulmonary artery have also been studied, due to the anatomical proximity of LMCA to these structures. Cases of serious LMCA damage have been identified.

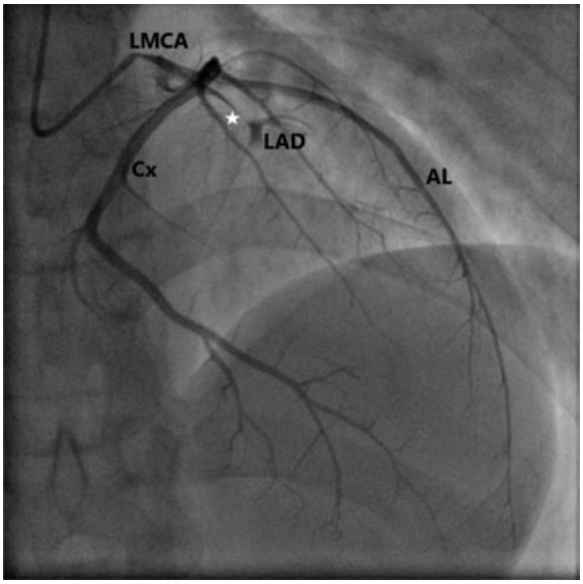

FIGURE 1 Angiographic image of ablation catheter-induced LMCA dissection with LAD occlusion and preserved flow in Cx and AL. Asterisk shows the point of LAD subocclusion. AL, anterolateral artery; Cx, circumflex coronary artery; LAD, left anterior descending artery; LMCA, left main coronary artery[23]

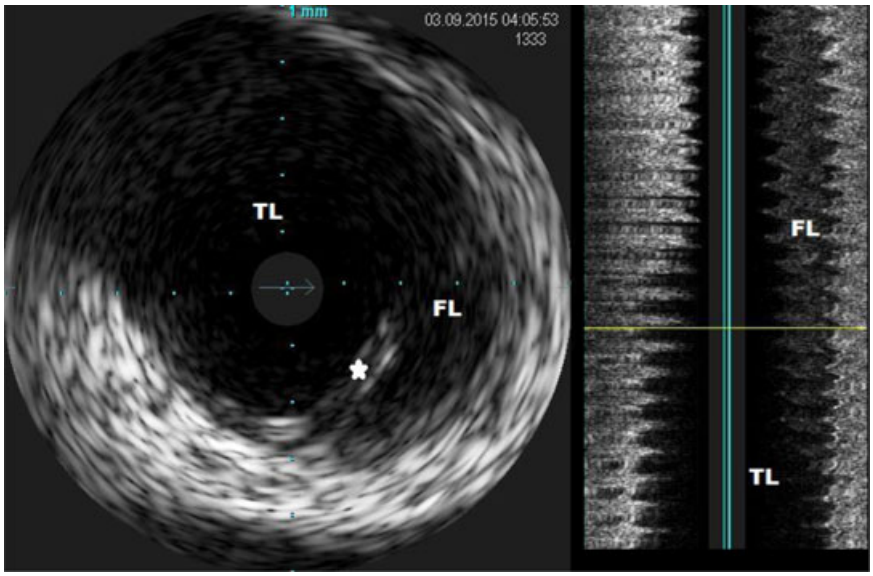

FIGURE 2 Intravascular ultrasound images of dissection entry site with intimal flap (marked with an asterisk) in the left main coronary artery. FL, partially thrombosed false lumen of dissected LMCA; LMCA, left main coronary artery; TL, compressed true lumen of LMCA[23] [Color figure can be viewed at wileyonlinelibrary.com]

Wide and short LMCA can easily be penetrated by an ablation catheter beyond the bifurcation up to its main branches, leading to their damage while at the same time leaving LMCA intact. Thus, to further evaluate the risk of direct mechanical trauma to coronary ostia in retrograde procedures, cases of ostial or proximal LAD and Cx injury, certainly or possibly attributed to catheter insertion into LMCA, have additionally been studied.

3 | RESULTS

In total, 22 reports of severe LMCA injury related to catheter ablation have been found, ranging from 1993 to 2018.[1,2,9–11,15,16,18,23–36] Additionally, four reports of serious ostial or proximal LAD and Cx damage have also been identified.[17,19,37,38] In this group, retrospective review of the angiograms suggested that it had been induced by a deep insertion of an ablation catheter into a short LMCA, which itself had been left unharmed. These patients were not included in the statistical analysis. The data of 22 patients with LMCA injury and of the four patients with LAD and Cx direct mechanical trauma are summarized in Table 1. Two reports of "aborted" LMCA injury have been published. In one patient, an attempt at RF ablation of VT originating in the high-posterolateral LVOT near LMCA produced chest discomfort and transient ST-segment elevation in the anterior precordial leads.[39] Although cardiac catheterization showed no abnormalities of the left coronary artery system, the procedure had to be terminated because transient LMCA irritation was suspected. Another description involved ST-segment elevation in septal and lateral leads during application of cryoenergy in the left coronary cusp 5 mm below LMCA ostium.[40] Electrocardiogram (ECG) changes resolved within 30 seconds, so after repeat angiography and catheter repositioning far away from LMCA, cryoablation was continued without further complications. The authors concluded that transient LMCA obstruction occurred due to ice formation or spasm.

In the group of 22 patients with ablation-related LMCA injury, the in-hospital mortality rate of 19 acute and subacute cases was 32%. Of all six deaths, five occurred among 10 patients treated in the years 1993 to 1997. In the remaining 12 patients, in whom catheter ablation was performed between 2008 and 2018, only one fatal outcome was observed. The degree of lumen obstruction and the presence of residual flow in the LMCA certainly has an impact on the hemodynamic condition of a patient; however, it is not the only factor influencing survival. In the present analysis, LMCA occlusion occurred with a comparable frequency both in patients who survived and in those who died. In the group with the nonchronic presentation, in six patients term "dissection" or "thrombus" was used, without further information whether coronary flow was preserved. In at least three of the six fatal cases, LMCA occlusion was found in angiography; in two patients "thrombus" and "dissection" was reported, in one patient residual flow was preserved. In 62% of 13 nonchronic patients with a positive outcome, LMCA occlusion was described; in one patient 90% stenosis was found and in the rest "dissection" was reported. Of the three chronic cases, one patient had "critical stenosis," one "90% narrowing" and in one LMCA was occluded.

As some patients' data were retrieved from multicenter registries or short abstracts, the details of the clinical course were not available for all cases. The group of patients with acute and subacute serious LMCA injury, whose initial clinical presentation was known, comprised of 14 cases. Of this number, in six patients cardiogenic shock or severe hypotension requiring vasopressors and/or intra-aortic balloon pump (IABP) was diagnosed. In seven cases, life-threatening ventricular tachycardia, ventricular fibrillation, electrical storm, or cardiac arrest with cardiopulmonary resuscitation was observed. In one patient, both cardiogenic shock and electrical storm occurred. Overall, in 86% of cases where the detailed description was available, the manifestation of LMCA injury was dramatic, requiring IABP insertion, defibrillation, resuscitation, and/or intubation. In only two patients the clinical course was less severe with chest pain and

TABLE 1 Patients with ablation-induced injury of LMCA and its branches

Patient no.	References	Year of report/ event	Age/sex/ CAD status	Vascular access	Energy type/ settings for thermal injury	Type of arrhythmia	Ablation site	Time of symptom onset	Clinical presentation	Angiographic findings	Suspected mechanism of injury	Treatment	In-hospital outcome	Long-term outcome/ months
1	Kosinski et al[24]	1993	17/M	Transaortic	RFA	AVRT—left-sided AP	LV	Acute: 15 min after the procedure	VT, anterior STEMI	LMCA occlusion	Catheter-induced direct mechanical trauma	PCI-balloon angioplasty to restore flow, then immediate CABG	Died of cerebrovascular accident after 1 wk, awaiting cardiac transplantation	…
2	Lesh et al[25]	1993	NA	Transaortic	RFA	AVRT—left lateral AP	LV	Subacute: 12 h	Anteroseptal AMI in ECG and echocardiography with cardiac enzymes rise	LMCA dissection and contained perforation with extrinsic hematoma compressing LAD	Catheter-induced direct mechanical trauma	Conservative, LMCA patent in repeat CAG 2 d later	Survived	3 mo after ablation, CABG performed due to expanding pseudoaneurysm of LMCA
3	Scheinman[1]	1995/ 1989-1993	NA	NA, probably transaortic	NA	AVRT—AP	Probably LV	Subacute: 24 h	NA	LMCA occlusion	NA	PCI (probably balloon angioplasty)	Survived	NA
4	Hope et al[15]	1995	40/F	Transaortic	Only mapping performed	AVRT—left posteroseptal AP	LV	Subacute: 12 h	Chest pain, anterolateral STEMI, cardiogenic shock	LMCA thrombotic occlusion	Catheter-induced direct mechanical trauma	PCI-perfusion balloon angioplasty with urokinase infusion	Survived	NA
5	Pons et al[18]	1997/ approx. 1995	24/M	Transaortic	RFA	Idiopathic LV VT	LV	Chronic: 2 y	Exertional angina	LMCA chronic occlusion; during CABG LMCA appearance suggestive of a dissection	Catheter-induced direct mechanical trauma	CABG	Survived	NA

(Continues)

TABLE 1 (Continued)

Patient no.	References	Year of report/ event	Age/sex/ CAD status	Vascular access	Energy type/ settings for thermal injury	Type of arrhythmia	Ablation site	Time of symptom onset	Clinical presentation	Angiographic findings	Suspected mechanism of injury	Treatment	In-hospital outcome	Long-term outcome/ months
6	Friedman et al[26]	1997	37/F	Transaortic	RFA, energy settings NA	Idiopathic outflow tract VT	High antero-septal LVOT, just beneath aortic valve	Acute, immedi-ately after RF applica-tion in LVOT	NA	LMCA abrupt occlusion; "extrinsic compression of the LMCA, without evidence of intraluminal thrombus or dissection"	Thermal injury	PCI-stenting	Survived	NA
7	Janeira[16]	1998	30/F	Transaortic	RFA	AVRT—left lateral AP	LV	acute: 30 min after pro-cedure	Chest pain, anteroseptal AMI, electrical storm with prolonged CPR	LMCA dissection with alternate Cx/LAD occlusion, confirmed in postmortem	Catheter-induced direct mechanical trauma	CABG	Died; prolonged CPR while awaiting CABG, considered brain-dead 48 h later	…
8	Calkins et al[2]	1999/ 1992-1995	56/F, known CAD with EF 38%	Transaortic	RFA	AVRT—left lateral AP	LV	acute: during pro-cedure	NA	LMCA dissection	Catheter-induced direct mechanical trauma	NA	Died	…
9	Schaffer et al[27]	2000/ 1991-1996	13/M	Transaortic and transseptal	RFA, energy settings NA	AVRT—left-sided AP	LV	<1 d	NA	LMCA thrombus	Thermal injury; energy delivered within or adjacent to the artery	NA	Died	…
10	Calkins et al[28]	2000/ 1995-1997	63/M, known CAD	Transaortic	RFA	VT (scar-related VT)	LV	Acute: 30 min after pro-cedure	Cardiogenic shock	99% LMCA subocclusion	Coronary embolus (ACT subtherapeu-tic) vs catheter-induced direct mechanical trauma	PCI (balloon/ stent-unknown)	Died of cardiogenic shock	…

(Continues)

TABLE 1 (Continued)

Patient no.	References	Year of report/ event	Age/sex/ CAD status	Vascular access	Energy type/ settings for thermal injury	Type of arrhythmia	Ablation site	Time of symptom onset	Clinical presentation	Angiographic findings	Suspected mechanism of injury	Treatment	In-hospital outcome	Long-term outcome/ months
11	Kharrat et al[29]	2008	38/F	Transaortic	RFA, energy settings NA	AVRT—left postero-lateral AP	LV	Acute: at the end of pro-cedure	Anterior STEMI, VF during PCI	LMCA thrombotic occlusion	Thermal injury; application near LMCA	PCI-stenting	Survived	NA
12	Yalin et al[30]	2010/ 2008	56/M	Transaortic	RFA	AVRT—left anterolat-eral AP	LV	Acute: at the end of pro-cedure	Chest pain, anterior STEMI	90% LMCA thrombotic stenosis	Catheter-induced direct mechanical trauma	PCI-stenting	Survived	1-mo FUp: CT angiogra-phy- stent patent
13	Diaz-Infante et al[31]	2012/ 2011	NA	Transseptal	NA	AFib	LA	Acute/ subacute	NA	LMCA thrombotic occlusion	NA; thromboem-bolus suspected	NA	Died	…
14	Kulawik et al[32]	2012	44/F	Transaortic	Before energy application	AVRT—left postero-lateral AP	LV	Acute: during pro-cedure	Chest pain, anterior STEMI, electrical storm during PCI, intubation	LMCA dissection with mid-LAD and proximal Cx occlusion	Catheter-induced direct mechanical trauma	PCI-stenting (two stents)	Survived	14-mo FUp: in CAG stents patent
15	Wacinski et al[33]	2013/ 2009	28/F	Transaortic	RFA, (50 W, 60°C, 43 s)	Idiopathic LVOT VT	LVOT	Acute: during pro-cedure	Cardiac arrest, CPR	LMCA occlusion	Catheter-induced direct mechanical trauma with RF-energy delivery	PCI-stenting, 1st stent dislocated into LM ostium and throm-bosed	Survived	12-mo FUp: 64-slice CT-stent patent, 24-mo FUp: asympto-matic
16	JACC[34]	2014	Middle-aged/F	Transaortic	NA	Left-sided AP	LV	Subacute: several hours after pro-cedure	Chest pain, congestive heart failure, hypotension, anterior STEMI	LMCA thrombotic occlusion	Catheter-induced direct mechanical trauma (vs late thromboem-bolism)	PCI-balloon angioplasty	Survived	12-mo FUp: asympto-matic

(Continues)

TABLE 1 (Continued)

Patient no.	References	Year of report/ event	Age/sex/ CAD status	Vascular access	Energy type/ settings for thermal injury	Type of arrhythmia	Ablation site	Time of symptom onset	Clinical presentation	Angiographic findings	Suspected mechanism of injury	Treatment	In-hospital outcome	Long-term outcome/ months
17	De Maria et al[9]	2015	31/F	Transaortic	RFA, 1 application (30 W, 48°C, 5 s), irrigate-tip catheter	Focal atrial tachy-cardia	LCC, 1-2 cm below LMCA	Chronic: symp-toms 2 mo after RFA, CAG at 4 mo	Angina, dyspnea	Critical ostial LMCA stenosis, constrictive remodeling in IVUS	Thermal injury due to energy delivery adjacent to LMCA	PCI-stenting	Survived	…
18	Doshi[35]	2015	50/F	Transaortic	RFA	Idiopathic LVOT VT	LVOT	Acute: during pro-cedure	Chest pain, electrical storm, CPR	LMCA distal occlusion at bifurcation	Catheter-induced direct mechanical trauma	PCI-stenting due to acute recoil after balloon angioplasty	Survived	Several years of FUp: stent patent in CAG
19	Yue-Chun et al[10]	2016	50/M, no CAD	Transaortic	RFA, 1 application (30 W, 43°C, 180 s), 3 applications (40 W, 180 s) irrigate-tip catheter	Idiopathic PVCs	LCC: approx. 10 mm from LMCA ostium	Chronic: 4 mo	NSTEMI with ST-segment elevation in aVR, with 3-wk history of exertional angina	Normal LMCA in CAG after ablation, 4 mo later 60% LMCA stenosis, 90% proximal LAD stenosis	Thermal injury due to energy delivery adjacent to LMCA	PCI-stenting	Survived	10-mo FUp: coronary CT: stent patent, 12-mo FUp: asympto-matic
20	Ielasi[36]	2017/ 2009	40/M	Transaortic	RFA	AVRT—AP	LV	Acute: during pro-cedure	Chest pain, STEMI, cardiogenic shock, electrical storm, intubation	LMCA dissection with LAD and Cx ostial occlusion	Catheter-induced direct mechanical trauma	PCI-stenting	Survived	NA
21	Klaudel[23]	2017/ 2015	27/M	Transaortic	RFA	AVRT—left-sided AP	LV	Subacute: pain started on the day of RFA, readmit-ted 2 d later	Anterior STEMI with low-output state	In IVUS distal LM dissection with LAD occlusion and preserved flow in Cx	Catheter-induced direct mechanical trauma	PCI-stenting	Survived	12-mo FUp: stent patent in CAG; ICD implanted due to VF and cardiac arrest

(Continues)

TABLE 1 (Continued)

Patient no.	References	Year of report/ event	Age/sex/ CAD status	Vascular access	Energy type/ settings for thermal injury	Type of arrhythmia	Ablation site	Time of symptom onset	Clinical presentation	Angiographic findings	Suspected mechanism of injury	Treatment	In-hospital outcome	Long-term outcome/ months
22	Kaneko et al[11]	2017	70/F, no CAD	Transaortic	RFA	PVCs	LCC	Acute: during procedure	Severe hypotension, junctional escape rhythm	LMCA dissection involving LAD and Cx in IVUS, 4-d repeat CAG with stenosis improvement	Catheter-induced direct mechanical trauma	Conservative: vasodilators, IABP	Survived	3 mo later NSTEMI with cardiogenic shock, LMCA subtotal occlusion, treatment: PCI-stenting
23	Calkins et al[17]	1991/ 1990	NA	Transaortic	RFA, energy settings NA	AVRT—left free-wall AP	LV	Acute: during procedure	Lateral AMI	Cx occlusion—thrombosis	Direct thermal and mechanical injury by ablation catheter with energy delivery within Cx	PCI (probably balloon angioplasty)	Survived	13-mo FUp: asymptomatic
24	Wieczorek et al[19]	2005	46/F	Transaortic	RFA	AVRT—left lateral AP	LV	Chronic: 8 y after ablation	Progressive chronic heart failure	LAD occlusion with fistula to RV proximal to occlusion	Catheter-induced direct mechanical trauma	Optimal medical treatment	Survived	NA
25	Yildiz et al[37]	2014	38/M	Transaortic	RFA	AVRT—left lateral free-wall AP	LV	Acute: 5 min after procedure	Chest pain, anterolateral STEMI	Proximal LAD occlusion far from ablation site	"Dissection of vulnerable atherosclerotic plaque"—unlikely, as RF application far from LAD, rather catheter-induced mechanical trauma	PCI-stenting	Survived	NA

(Continues)

TABLE 1 (Continued)

Patient no.	References	Year of report/ event	Age/sex/ CAD status	Vascular access	Energy type/ settings for thermal injury	Type of arrhythmia	Ablation site	Time of symptom onset	Clinical presentation	Angiographic findings	Suspected mechanism of injury	Treatment	In-hospital outcome	Long-term outcome/ months
26	Kordic et al[38]	2018	36/M	Transaortic	Energy not delivered	Fascicular left VT	LV	Acute: during LV mapping	Anterolateral STEMI, anxiety, sweating	Ostial LAD occlusion due to dissection	Catheter-induced direct mechanical trauma	PCI-stenting	Survived	15-mo FUp: stent patent in CAG

Abbreviations: ACT, activated clotting time; AFib, atrial fibrillation; AMI, acute myocardial infarction; AP, accessory pathway; AVRT, atrioventricular reciprocating tachycardia; CAD, coronary artery disease; CABG, coronary artery bypass grafting; CAG, coronary angiography; CPR, cardiopulmonary resuscitation; CT, computed tomography; Cx, circumflex artery; EF, ejection fraction; IABP, intra-aortic balloon pump; ICD, implantable cardioverter-defibrillator; IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCC, left coronary cusp; LV, left ventricle; LVOT, left ventricular outflow tract; NA, not available; NSTEMI, non–ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; FUp, follow-up; PCI, percutaneous coronary intervention; PVC, premature ventricular complex; RFA, radiofrequency ablation; RV, right ventricle; VF, ventricular fibrillation.

ST-segment elevation, and in both these cases, LMCA flow was preserved, with nonocclusive lesion found in coronary angiography.

Three of 22 patients (14%) had late onset of symptoms, ranging from 2 months to 2 years. At least five patients (23%) had a subacute presentation (12-24 hours after the procedure), and in 12 patients (55%) symptoms manifested acutely (during the procedure or up to 30 minutes after its termination). In the remaining two cases, only nonchronic in-hospital presentation was established without the exact time frame. Presentation time did not correlate with survival, that is, delayed onset did not predict the fatal outcome. Of all six patients who died in hospital, at least four had acute symptom manifestation (in two other patients, the presentation was non-chronic, without available details). However, only one of the four deceased patients with an acute presentation developed symptoms during the procedure. The other three became symptomatic 15 to 60 minutes after ablation completion, so they had to be transferred back to the electrophysiology/catheterization laboratory.

In the overall population of 22 patients, in 14 (64%) unintended catheter insertion into LMCA resulting in direct mechanical injury was certain or strongly suspected (in eight cases, the angiographic and/or IVUS image was identified as "dissection"), with RF-energy delivered intracoronary in two of them. Of the remaining eight patients, in five cases (23%), thermal injury due to energy application close to LMCA origin was inferred (in one patient the authors did not know whether RF energy was applied within or adjacent to LMCA), in one patient LMCA thromboembolic occlusion was assumed, and in two cases the alleged mechanism was not indicated. In all cases of LMCA thermal injury, with energy delivered either intraluminally or in the proximity of the vessel, the RF current was applied. No reports of serious LMCA damage attributed to cryoablation have been found. Inadvertent LMCA penetration by an ablation catheter, with either LAD or Cx occlusion, was the presumed cause of CAI in the four additionally studied cases, in which LMCA itself had been spared.

Of all studied cases, 18 (82%) involved ablation in LV/LVOT (13 AVRT and five VT), three procedures were performed in the aortic cusps (two PVCs and one focal atrial tachycardia), and one patient underwent atrial fibrillation ablation. All 22 procedures were performed with fluoroscopy control, and in the three ablations targeting the left sinus of Valsalva, preprocedural angiography was obtained and intracardiac echocardiography was not utilized.[9–11]

In most patients, LMCA injury became apparent only after ECG changes and/or severe symptoms developed, and the operator was unaware of inadvertent coronary artery penetration, ablation catheter dislocation, or energy application too close to the coronary ostium. The mechanism of trauma was speculated in the post hoc analysis of a given case. Overall, only in four cases of 22 (18%) studied, ablation catheter improper position or its dislodgement was quickly recognized. In two of them, a catheter was expelled from LV/LVOT into the ascending aorta during RF application.[16,33] However, only in one of these cases LMCA penetration was immediately realized as the patient sustained cardiac arrest.[33] In the other two patients, a catheter was seen to enter LMCA during an attempt to prolapse the aortic valve, which was then successfully

crossed and the ablation procedure was continued until severe symptoms appeared.[25,35]

Of 19 cases with an acute and subacute LMCA injury, the data considering applied treatment were not available for three patients who died. Among 16 patients for whom therapy details were sufficient, only two underwent urgent CABG and both died.[16,24] In another two cases conservative treatment was chosen and both patients had to be readmitted 3 months after the initial event. One of them was operated due to an expanding LMCA aneurysm.[25] The other patient was rehospitalized due to myocardial infarction with cardiogenic shock that was treated with LMCA stenting.[11] The remaining 12 patients underwent urgent percutaneous coronary intervention, and in at least eight of them LMCA stenting was performed, with all 12 surviving the adverse event. In one patient, stenting of a coagulated LMCA proved to be a challenging procedure, leading to stent dislocation and its subsequent intraprocedural thrombosis.[33] In another case, 3 hours after emergent LM-LAD stenting, inferolateral ST-segment elevation myocardial infarction with the low-output state was diagnosed. Repeat angiography revealed dissection from LMCA into Cx and first-diagonal branch spasm.[36]

In at least four patients, the authors mentioned that intra-aortic balloon counterpulsation had been used.[11,15,33,36] In three cases, glycoprotein IIB/IIIA receptor antagonist abciximab (potent antiplatelet agent) was administered.[29,32,33] In one patient with LMCA dissection, and two others with ostial LAD occlusion caused by deep LMCA penetration, aspirational thrombectomy was attempted, but no thrombus was retrieved.[23,37,38]

Despite dramatic presentation, no less than five patients with symptoms developing during or at the end of ablation had normal left ventricle function preserved after urgent angioplasty.[26,29,30,32,35] In two of them, cardiac enzymes rise was not observed even though one patient was resuscitated during the procedure.[35]

4 | DISCUSSION

LMCA is a short vessel with a relatively large diameter of 3.5 to 5 mm and as such is naturally protected against thermal injury during RF ablation, thanks to the convective cooling phenomenon. LMCA trauma is a rare complication of catheter ablation. Due to the large territory of LMCA perfusion, its damage constitutes the most serious of all coronary artery injuries complicating the procedure. The analyzed group is the largest cohort of ablation-related LMCA injuries studied to date. The small sample size precludes strong generalizations; however, it enables to make some observations and conclusions, considering the mechanism, clinical course, and therapy.

4.1 | Ablation site

Theoretically, LMCA occlusion can occur both during transvenous and transaortic (or transseptal) ablation. In a study by Vaseghi et al,[41] the relationship between RVOT and LMCA was assessed by coronary angiography during RVOT VT ablation, by computed tomography (CT) angiography, four-dimensional echocardiography during open heart surgery (on a beating heart) and by intracardiac echocardiography (ICE). The distance from RVOT to LMCA was 3.8 ± 1.2, 4.1 ± 1.9, 3.4 ± 0.35, and 3.8 ± 0.45 mm, respectively. Therefore, the authors concluded that coronary angiography or ICE should be considered when ablation sites are located in the high-septal RVOT. As noted by Ouyang et al,[42] the so-called "superior septal" aspect of RVOT, that is, the posterior wall of the subpulmonary infundibulum, is in fact not septal as its epicardial surface is adjacent to the left and right aortic sinuses, with some extracardiac tissue interposed in between. Walsh et al[43] performed an anatomic study to assess the relationship of LMCA to the neighboring structures in CT coronary angiograms of 100 patients investigated for chest pain. They found that LMCA coursed within 5 mm of the anterior left atrial endocardium and/or base of left atrial appendage in 49% of cases (within 2 mm in 17%), and from the pulmonary artery in 90% (within 2 mm in 43%), though rarely close to RVOT. In another study the anatomic relationship of the pulmonary root to the coronary arteries was evaluated using CT coronary angiograms.[44] The authors determined that the left adjacent pulmonary sinus was located within 5 mm of LMCA in 67% of cases, and in 19% within 2 mm distance (within 5 mm of LAD in 87%, while in 36% within 2 mm). The distance between LMCA and the adjoining heart cavities and great arteries may become smaller in patients with left atrial enlargement due to atrial fibrillation or chronic heart failure, as well as in case of pulmonary artery dilation in the setting of pulmonary hypertension. LMCA compression syndrome is increasingly recognized in patients with pulmonary hypertension and concomitant angina. Theoretically, thermal injury during ablation in the left atrium, the left atrial appendage, RVOT, and the pulmonary artery is also more likely when LMCA is a wide and long vessel. If LMCA is short and its bifurcation is close to the vessel ostium, it is LAD that takes a long course near the pulmonary artery/RVOT and the left atrial appendage (while Cx runs in the proximity of the left atrium and the left atrial appendage). These findings suggest that LMCA is potentially within the radius of necrosis during ablation of premature ventricular complexes and idiopathic VT arising from RVOT (or myocardial extensions into the pulmonary artery), atrial fibrillation or atrial tachycardia ablation, and left atrial appendage electrical isolation (Figure 3). Despite LMCA intimate relation to the above-mentioned structures, no reports of the vessel damage during arrhythmia ablation have been found though other coronary arteries have been affected, that is, LAD in RVOT VT ablation and Cx during ablation at the base of the left atrial appendage.[45,46] Although CAI has not been reported in large worldwide surveys on atrial fibrillation ablation, the fact that in almost half of the population with normal coronary anatomy studied by Walsh et al[43] LMCA coursed within 5 mm of the left atrium and/or its appendage, raises special caution due to the growing numbers of these procedures.[47]

In the present study, the left ventricle and LVOT were the most common (18 cases, 82%) locations of transaortic ablation complicated by LMCA injury, and only three reports of LMCA damage during procedures performed in the left sinus of Valsalva have been found

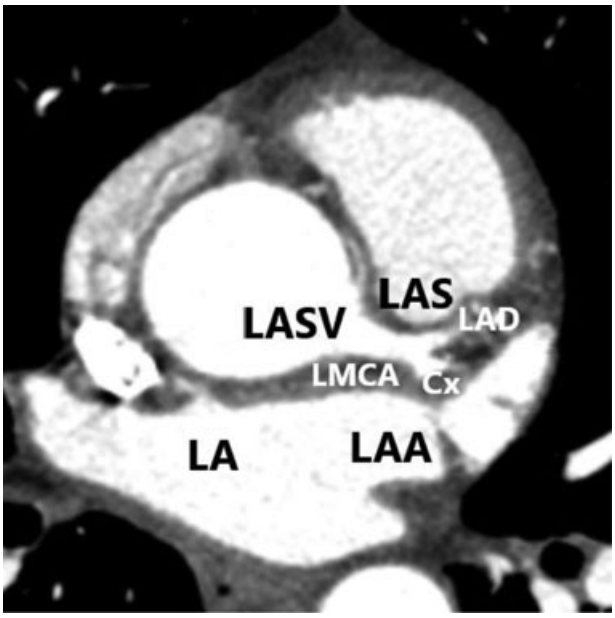

FIGURE 3 Axial CT image of the heart—transverse reconstruction showing anatomic relation of LMCA to the adjacent structures. The distance from LMCA to LAA and LAS is 5.15 and 2.30 mm, respectively. CT, computed tomography; Cx, left circumflex coronary artery; LA, left atrium; LAA, left atrial appendage; LAD, left anterior descending artery; LAS, left adjacent sinus of the pulmonary artery; LASV, left aortic sinus of Valsalva; LMCA, left main coronary artery

despite catheter manipulation and energy delivery in direct proximity to the left coronary artery ostium. Two cases of ostial RCA injury sustained during idiopathic VT RF ablation in the right coronary cusp have also been published.[12,13] Sinus of Valsalva ablation was introduced only in 1994 and even with its wider adoption in later years it still remains a procedure of limited application. In recent years, the aortic cusp ablation has been performed for the elimination of premature ventricular complexes or idiopathic VT foci, focal atrial tachycardia, and accessory pathways. In the case series of aortic sinuses ablation by Hoffmayer et al[6] (35 patients with ventricular arrhythmias) and Yamada et al[7] (44 patients with ventricular arrhythmias), as well as in the literature review by Letsas et al[8] (35 patients with septal bypass tracts), no incidents of CAI were reported. Low incidence of coronary ostia damage during aortic cusp ablation reflects the smaller number of procedures performed but may suggest that adequate caution is exercised because of the coronary artery proximity. However, the procedure also involves mapping and sometimes energy delivery in LV/LVOT and as such requires aortic valve crossing, with the inherent risk of catheter springing into LMCA.

4.2 | Mechanism

In the present analysis, direct mechanical trauma (with or without radiofrequency current application) inflicted by unintentional LMCA cannulation with an ablation catheter was most often reported as a suspected mechanism of the vessel injury. LMCA penetration usually occurred while crossing and recrossing the aortic valve, or when a catheter dislodged from LV/LVOT during mapping/ablation of bypass tracts or ventricular arrhythmias. In a report of ICE-guided RF ablation of idiopathic VT performed in subvalvular LVOT (close to the left coronary cusp, in the area of aortomitral continuity), the ablating electrode was seen to slide toward the left coronary cusp during three applications in the five treated patients.[48] A 7-Fr ablation catheter can also accumulate elastic energy while attempting to prolapse the aortic valve or during its removal. This energy added to the catheter-tip stiffness can cause significant mechanical trauma to the coronary ostia even without energy delivery. In most cases of direct mechanical injury, vessel dissection was identified, with the artery perforation and pseudoaneurysm in one patient.[26] Unlike coronary angioplasty-related LMCA damage, no reports of the dissection retrograde propagation into the left sinus of Valsalva or ascending aorta have been found. This is most probably due to the fact that although an ablation catheter is stiff enough to induce aortic dissection and aortic valve rupture, automated contrast injection during coronary angiography facilitates retrograde false lumen expansion into the ascending aorta. Catheter insertion into LMCA is not always traumatic and it may go unnoticed as not all incidents cause actual injury or manifest acutely.[9,18,49] Sometimes a catheter is intentionally advanced into LMCA ostium during three-dimensional (3D) electroanatomical mapping to establish and tag its position. Pace mapping with a soft-tip 6-Fr deflectable catheter is also safely performed within LMCA.[50] In contrast to air embolism typically affecting RCA, mechanical trauma induced by an ablation catheter during the aortic valve crossing shows a predilection for LMCA. This may be explained by the aortic valve crossing technique and the fact that an ablation electrode is naturally oriented by the arch of the ascending aorta towards the left sinus of Valsalva. When LMCA is a short and wide vessel, LAD, Cx, ramus intermedius or first-diagonal branch can be selectively traumatized during catheter unintentional insertion.[17,19,37,38]

The second most common cause of ablation-related LMCA damage was thermal injury due to RF energy delivery in LV/LVOT or the left coronary cusp, adjacent to LMCA origin. RF current was implicated in all cases of LMCA thermal injury, both when energy was applied directly in the artery or close to the vessel. No cases of serious LMCA damage attributed to cryoablation have been identified and only one report of LMCA transient irritation during cryoapplication in the left coronary cusp has been published.[40] Cryoablation offers the possibility of creating reversible lesions during cryomapping; cryolesions are also less thrombogenic and lesion expansion has not been observed. With a better safety profile compared with RF procedures, cryothermy is often chosen to be performed in close proximity to coronary arteries. In a study of AP epicardial ablation in coronary veins performed within 2 mm and 3 to 5 mm of a coronary artery, in repeat angiograms CAI was found in 50% and 7%, respectively, when RF energy was used.[5] No CAI was observed for cryoenergy applied within 5 mm of a significant coronary artery, though at the cost of lower procedure success rate. Although cryocatheters are more difficult to handle than RF catheters, they are more stable due to the tip adherence

to myocardial tissue which reduces the risk of catheter dislodgement during systolic-diastolic motion, respiration, or patient's movement. Despite all the advantages and favorable study outcomes, cases of CAI attributed to cryoablation have been published.[4]

Thromboembolic occlusion was the third and the least frequent mechanism of LMCA injury and it occurred in only one patient during LV ablation (the possibility of mechanical damage was also considered).[28] With standard heparinization protocols and repeated ACT tests, thromboembolism has become an uncommon complication of retrograde procedures. Coronary arteries are naturally protected from catheter thrombi or endocardial char due to the sharp angle of their departure from the aortic bulb (eg, coronary embolism in patients with atrial fibrillation is rare, compared with transient ischemic attack and stroke).[47]

4.3 | Clinical course

One of the most important findings of this review is the significant number of nonacute cases (no less than eight out of 22), and the high percentage of patients in whom LMCA injury initially went unnoticed (only in 18% catheter dislodgement or improper position was immediately recognized). A serious injury of LMCA or a major coronary branch with a significant flow compromise is unlikely to be asymptomatic. Delayed occlusions in some of the analyzed cases confirm that in some patients the progression of coronary obstruction may be protracted. Disruption of the LMCA endothelial layer may remain silent during procedural heparinization, and after unfractionated heparin ceases to act; especially with rebound hypercoagulability phenomenon, thrombosis may ensue. Even in the case of LMCA dissection, the course may also be protracted with delayed propagation of intramural hematoma and/or thrombus formation.[25] If LMCA stenosis grows gradually (or leads to chronic occlusion over time) as a consequence of acute subclinical trauma, collateral circulation may develop in time to save the patient.[18] Before discernible coronary stenosis develops, changes in the wall structure not encroaching on the vessel lumen are not detectable by angiography. IVUS or optical coherence tomography (OCT) is the appropriate imaging methods to visualize artery remodeling; however, even these modalities are not able to assess prognosis in the absence of a hemodynamically significant narrowing.[9,11,13] In a pig study, intimal hyperplasia was detected in IVUS between 3 and 6 months after RF ablation, without significant change in 9- and 12-month IVUS.[51] This may suggest that by 6 months the process of lesion maturation is finished. Whether healed postablation coronary injuries make the vessel more prone to atherosclerosis is not established.

In this review, some of the patients with subacute presentation were close to the time of discharge. Out-of-hospital sudden cardiac death may also be the manifestation of ablation-related CAI, particularly when a large vessel has been affected. Cases of delayed coronary artery occlusion after catheter ablation manifesting as ventricular fibrillation have been described. Of 22 patients with a serious LMCA injury, as many as five were readmitted after the initial ablation procedure due to myocardial ischemia. Among them, three had chronic presentations after having undergone catheter ablation, with an uncomplicated in-hospital course.[9,10,18] Two other experienced lesion progression after initial conservative therapy of LMCA damage.[11,25] One of the latter was readmitted in shock due to non-ST-segment elevation myocardial infarction (NSTEMI) caused by subtotal LMCA occlusion.[25]

The fact that more than one-third of the patients (37%) had a nonacute presentation and only in four cases the incident was immediately noticed, raises several important issues. Patients after procedures with a high risk of coronary artery damage, particularly the ablation in the aortic cusps and with the aortic valve crossing, require prolonged electrocardiographic monitoring. If LMCA or RCA forceful penetration is noticed or suspected, extended hospital stay and outpatient follow-up with stress tests, repeat angiography or coronary CT should be considered. Normal coronary angiography performed immediately after the procedure does not exclude subclinical coronary artery injury. IVUS and/or OCT are better suited to unambiguously rule out LMCA dissection, its wall edema, and serious intimal disruption. A high level of suspicion is warranted in patients with a history of ablation involving aortic valve crossing or applications in direct proximity of LMCA. Angina or congestive heart failure symptoms in such cases should prompt myocardial ischemia workup.

4.4 | Treatment

Percutaneous angioplasty is the quickest way to restore normal blood flow within LMCA, especially when a patient is still in the laboratory and femoral arterial access is maintained. In acute and subacute cases, especially with hemodynamic compromise, CABG should be reserved only for lesions not amenable to PCI. Direct stenting seems to be the best treatment option, especially in case of both mechanical and thermal injury, when the lumen is not only dissected or compressed by intramural hematoma, but LMCA endothelium is burnt as well. If RF energy has not been applied endoluminally, expected restenosis rate after drug-eluting stent implantation should be lower than in the atherosclerotic calcified lesions, as the dissected artery wall is usually otherwise normal in young patients with AVRT or idiopathic VT.

When LMCA is damaged but patent, the dissection is localized and non–flow-limiting, and the patient is hemodynamically stable, CABG may be considered. In patients without hemodynamic collapse surgical treatment should be preferred when LMCA bifurcation is affected (especially when the two-stent technique is strongly anticipated), or when the dissection is retrogradely propagating into the aortic root. Studies have shown that PCI achieves better long-term results in ostial and mid-shaft LMCA lesions with only one stent technique used.[52] In chronic LMCA stenosis both PCI and CABG are an option, depending on lesion morphology, patient's condition, comorbidities, etc. In the latest meta-analyses of trials comparing PCI and CABG in unprotected LMCA disease, both treatment modalities demonstrated no difference in the composite endpoint of death, stroke, and myocardial infarction, with a higher rate of repeat revascularization in the PCI group.[53]

In the reviewed cases of LMCA injury, stent implantation has shown the best long-term effect as patients treated conservatively or with balloon angioplasty only required definitive therapy (either stenting or CABG) due to progressive narrowing of the affected vessel.[10,11,25] Similarly, in the two cited reports of RCA ostial damage by Kusa et al[12] and Araki et al,[13] balloon angioplasty was initially performed, with stents eventually implanted due to progressive stenosis after 18 and 15 months, respectively. In a literature review by Onsea et al,[54] in 50 out of total 54 cases of iatrogenic LMCA dissection complicating percutaneous coronary procedures, successful bailout stenting was performed, while the rest underwent CABG. Considering the fact that regardless of coronary dominance type, the major part of LV myocardium is supplied by LMCA, leaving its dissection for watchful waiting may pose too big a risk for a patient. As demonstrated by the report by Kaneko et al,[11] readmission may not be just due to exertional angina but cardiogenic shock as well. This is especially the case when LMCA has been affected by both mechanical and thermal damage. Mechanical dissection of a coronary artery with the superimposed thermal injury inflicted directly on intimal endothelium is bound to evoke a major inflammatory response. Animal studies of coronary artery injury involved external energy application adjacent to the vessel wall. No animal model exists for direct intimal burn; the closest approximation being renal artery denervation procedure. However, renal artery cross-sectional area is 2.5 times bigger than LMCA's; therefore, vessel wall edema and intravascular thrombus are much less likely to cause acute artery occlusion. Moreover, different RF energy settings are used, thus the studies of renal denervation cannot be extrapolated to coronary vasculature. The healing process and lesion evolution in case of the endothelial burn are unpredictable. Consequently, balloon angioplasty, even if acute vessel recoil is not observed, may prove inadequate.[12,13] For bare-metal and drug-eluting stents implanted to treat CAI only anecdotal long-term observations are available, (especially for cases of endoluminal RF energy delivery). However, in a 2-year follow-up, Wacinski et al[33] reported that despite both mechanical and thermal damage sustained, the LMCA stent was without restenosis. Similarly, in patients with mechanical LMCA injury described by Kulawik et al[32] and Klaudel[23] the stent was patent after 1 year, and even several years after the index procedure in the case published by Doshi et al.[35] Yue-Chun et al,[10] in repeat angiography after 10 months, also confirmed a good long-term result of LMCA stenting performed due to external thermal injury. If a conservative treatment or balloon angioplasty is chosen, scheduled or symptom-driven coronary angiography/CT and stress tests should be considered.

In cases of catheter-related LMCA and LAD dissection, aspirational thrombectomy proved futile, prolonging total ischemic time, and it is not recommended according to the latest recommendations due to the risk of coronary and cerebral embolism.[23,37,38] The haziness seen in a dissected artery may often be the result of an intramural hematoma rather than significant intraluminal thrombus burden. Thus, if LMCA dissection is certain, thrombectomy attempt may only delay reperfusion, and direct stenting should be preferred. If the angiographic image is highly suggestive of a large clot, aspirational thrombectomy may be considered, taking into account the risk of thrombus embolism from a catheter tip into the aorta, which is especially high for ostial lesions. In several of the analyzed cases, IABP was used as circulatory support. Nowadays, more potent Impella system is available, but the insertion of even the smallest device (Impella 2.5) through 13-Fr sheath takes more time than IABP. For bigger Impella devices, a surgical femoral arteriotomy is often needed, so it may potentially be used after urgent LMCA flow restoration in case of cardiogenic shock or electrical storm.

Pharmacological therapy after complicated ablation that required coronary stenting typically involves two antiplatelet agents, that is, acetylsalicylic acid (ASA) and clopidogrel/prasugrel/ticagrelor for 1 to 12 months. There is no standard therapy for cases of suspected subclinical LMCA injury, but many centers routinely prescribe ASA after left-sided ablation for 1 to 3 months, even if it was uncomplicated. Similarly, fractionated heparin or IV heparin is recommended for 12 to 24 hours after left-sided catheter ablation of ventricular tachycardia with overt heart disease, with ASA 80 to 325 mg/day for at least 1 month. Therefore, if conservative treatment is chosen for nonobstructive LMCA damage, heparin should be administered overnight or longer, with ASA or double antiplatelet therapy for at least 1 month. The same antithrombotic and antiplatelet therapy should be considered if RF applications too close to LMCA ostium or inadvertent LMCA penetration are suspected.

4.5 | Outcome

In-hospital mortality of patients with acute/subacute presentation in the present analysis was 32%. This is higher than 5.6% mortality cited in the literature review of iatrogenic LMCA dissections during coronary angioplasty published by Onsea et al,[54] but in such cases diagnosis is immediate and interventional cardiologists are ready to perform urgent bailout stenting. This boosts the survival even though patients undergoing PCI are more likely to be older or to have low ejection fraction, significant coronary artery disease affecting RCA, and serious comorbidities, all carrying the risk of unfavorable outcome. Retrograde ablations that almost exclusively account for LMCA injury also possess an advantage of ready arterial access in case of bailout angioplasty, but there is still some delay in diagnosis and LMCA catheterization. Acute mortality in a systematic review of 55 cases of catheter ablation-related CAI from the years 1992 to 2015 by Pothineni et al[20] was only 5.4%. The survival was much better due to minor arteries being affected in the majority of cases (only two cases of LMCA injury were included).

In the analyzed cohort, the patients were generally young with otherwise normal hearts, without congestive heart failure and/or ischemic heart disease. There were only two persons with known coronary artery disease, and they both died during or shortly after the complicated procedure.[2,28] Coronary arteries with atherosclerotic plaque are more prone to injury and chances of surviving LMCA damage are small if other coronary arteries are stenosed. There were

also two teenagers in the studied group, aged 13 and 17 years, both of which died in hospital.[24,27] Young age itself does not predict the unfavorable outcome, but ablation in LV/LVOT or aortic root may be challenging in smaller children due to relatively narrow space for catheter maneuvers and vigorous wall motion. Only one death occurred in patients treated after 2000, so there is clearly a trend towards better survival, probably reflecting gathered experience, common availability of stents and interventional cardiologists on 24/7 duty. Patients surviving the acute event for whom follow-up was available generally fared well in the long term. Urgently performed bailout procedures in some of the cases did not cause troponin elevation and wall-motion abnormalities.[35]

4.6 | Prevention

Considering the devastating consequences of ablation-related LMCA injury and high mortality of this complication, prevention is of utmost importance. Safety measures include better visualization, real-time imaging of catheter tip-LMCA distance, improved catheter stabilization, RF energy titration, use of a diagnostic coronary catheter to block LMCA ostium, and repeat angiography after procedure completion. Other simple precautions, such as monitoring relevant surface ECG leads at speed of 25 mm/s during the procedure, and performing 12-lead ECG immediately after ablation can easily be implemented. If during ablation in the subvalvular LVOT or the aortic cusps a sudden increase in the impedance and/or in temperature occurs, it strongly suggests catheter dislodgement into the coronary artery and the energy application should be discontinued immediately. It would seem prudent to schedule procedures with an increased risk of CAI early in the day and notify a coronary intervention team. Today, cardiology centers that perform ablations commonly have catheterization laboratories on-site, many of which are on 24/7 duty for ST-segment elevation myocardial infarction interventional treatment. However, in the case of acute LMCA occlusion, cardiogenic shock and cardiac arrest often occur within minutes, so the intervention has to be performed as an emergent procedure. If an electrophysiological and catheterization laboratory is not situated nearby, it would be advisable to keep a basic pack of coronary interventional equipment in the ablation room.

Three-dimensional electroanatomical mapping and fluoroscopy are widely used for tracking catheter position. If LV is entered, it is essential to use multiple fluoroscopic angulations to ensure ablation catheter proper location, especially while crossing the aortic valve with some effort. From the early days of aortic cusp ablation, reports of procedures safely performed with the guidance of fluoroscopy and electroanatomical mapping were published. In one such study, energy delivered by a 4-mm tip electrode was titrated to 25 W (with initial power setting of 15 W) and immediately turned off if even minimal dislodgement from the site of identical pace mapping (ie, showing QRS identical to the clinical VT morphology) was noticed.[55] However, nowadays more reliable methods are often considered when RF energy is to be applied in direct proximity of coronary ostia in the aortic cusps, or in the high LVOT beneath the aortic valve. Coronary angiography and ICE are typically used to precisely establish the ablation catheter relation to LMCA origin. Both imaging techniques have their proponents. Coronary angiography has been traditionally utilized to define simultaneously LMCA ostium, its course, and coronary flow. Conventional angiography or preprocedural CT angiography may also reveal coronary anomalies and the resultant atypical coronary artery course. A case series has been published where control coronary angiography was performed routinely 4 weeks after coronary cusp ablation, despite maintaining 10-mm safety margin.[56] ICE is more costly but is becoming more popular, as it allows for real-time, continuous, and concurrent visualization of an ablation catheter, the aortic sinus, the aortic valve, and coronary ostia, thereby enabling reliable measurement of catheter tip-coronary ostium distance. As suggested by Rillig et al,[57] ICE can also identify aortic wall plaques which at least in part may help prevent thromboembolic complications. In some centers, RF energy is delivered in the aortic cusps under continuous fluoroscopy to observe for catheter dislocation. ICE can replace this technique, thus minimizing the radiation dose. However, as pointed out by Walsh et al,[43] in 4% of patients LMCA takes an unusual inferior course, remaining within 5 mm of the left sinus of Valsalva. The authors caution that this may be overlooked if only ICE is utilized for LMCA detection. In suitable anatomical conditions, this obstacle may be overcome with Doppler flow imaging and incorporated into a 3D map.

There are no standard recommendations; therefore, the preferred imaging modality depends on a center's experience and expertise, and in patients with difficult visualization conditions one technique may supplement the other. Hoffmayer et al[6] reported that in a series of 35 aortic cusp ablations they performed coronary angiography only if in ICE the mapping catheter was within 10 mm of the coronary artery ostium (ie, in 9% of patients). The authors noticed a trend towards utilization of adjunctive angiography in the right coronary cusp procedures due to more challenging visualization of RCA ostium in ICE. Similarly, Jauregui-Abularach et al[58] performed ablation of LV summit arrhythmia from the left sinus of Valsalva, using coronary angiography to visualize LMCA ostium and its course only if ICE showed the distance of catheter tip to be less than 10 mm. ICE is also used to guide and monitor electrode position during RF ablation in subvalvular LVOT.[48] An alternative method to control the distance from a catheter tip to a coronary ostium during ablation in the Valsalva sinuses, not requiring additional vascular access, has been proposed.[59] The authors used the lumen of a cooled-tip catheter to perform repeat angiography for real-time assessment of its relation to a coronary artery. This technique has been preferred and safely used in our electrophysiological laboratory for the aortic cusp ablation, to ensure that the application site is far enough from the coronary artery ostium, with ICE reserved for pulmonary vein isolation procedures. For LV summit arrhythmia ablation (including transaortic failed cases), Ouyang et al[60] successfully performed RF applications in anterosuperior LVOT (5.1 ± 2.8 mm below the coronary cusps) via a transseptal approach with a reversed S curve of an ablation catheter, under the control of coronary angiography. The authors proposed that antegrade access may be used not only

for LVOT procedures but also as an alternative approach for ablation of ventricular arrhythmias from the left coronary cusp when the distance to the LMCA is below 5 mm or if the catheter position is unstable.

Different methods of integrating CT, magnetic resonance imaging, coronary angiography, and ICE images with the electroanatomical map are utilized, and with the continuous development of the merging software, their widespread use is likely to ensue. Development of ICE catheters with reduced size and higher image resolution and improvement of 3D technology will allow better image quality and eliminate the need for the ultrasound probe manipulation. Due to the anatomical relationship described before, additional visualization of LMCA course should also be considered when ablation is to target the leftward posterior high-septal aspect of RVOT, the posterior wall of the pulmonary artery (and its left adjacent sinus), the anterior left atrial endocardium, and the base of the left atrial appendage. The proximity of LMCA in some of the above-mentioned procedures is well recognized; for example, in a study of ablation of ventricular arrhythmias originating from the pulmonary cusps the authors titrated irrigated RF current settings to 40 W, 43°C, and 60 seconds for fear of damaging the left coronary artery.[61] Preprocedural CT angiography, transesophageal echocardiography, intraprocedural ICE guidance or coronary angiography may establish the close relation of these thin-walled heart cavities to LMCA in an individual patient, thus helping avoid potential complications.

According to recommendations, a distance greater than 5 mm from a coronary artery is safe, but in case of catheter instability caused by beating heart and respiratory movement many centers use a bigger margin of 10 mm.[56] Long sheaths that provide better catheter control in the ascending aorta and limit its dislocation from LV when mapping endocardium in LVOT below the left coronary cusp should be preferred. Cryoablation offers better stability, thanks to cryoadhesion of the catheter tip to the endocardium. This method has been demonstrated by McDonnell et al[40] as a safe alternative for the left coronary cusp ablation near LMCA ostium, with procedures performed as close as 5 ± 1 mm from LMCA center measured on ICE. Interestingly, a case of outflow tract tachycardia mapped inside LMCA (5 mm from its ostium) has been described.[50] The authors successfully performed a part-circumferential set of ablation lesions to avoid energy delivery in the vicinity of LMCA. In another case, ventricular tachycardia originating within LMCA ostium was successfully ablated by a transthoracic surgical approach, using cryoenergy.[49]

A 5-Fr Judkins diagnostic catheter is sometimes used to perform repeat angiography as well as to mark and block LMCA ostium throughout the ablation or during energy application.[7,42,57,62] It may be especially helpful when an ablating electrode is unstable and the risk of its dislodgement is deemed too high.[57] Some operators recommend frequent injections of contrast, that is, every 15 seconds, during RF energy delivery in the aortic coronary sinuses.[7] Leaving diagnostic Judkins catheter in LMCA ostium efficiently prevents its unintentional penetration but requires additional puncture of the femoral artery with all its inherent risks. The presence of another catheter may also restrict precise manipulation of an ablation catheter. If a blocking catheter is used, coronary artery irrigation with chilled saline during energy application may be considered, a strategy which has proved effective in preventing heat-induced coronary lesions in animal studies of epicardial RF ablation.[63]

RF energy titration and use of smaller tip catheters is often recommended to reduce lesion size and avoid CAI. As advocated by Rillig et al,[57] usual settings for conventional RF ablation within the sinuses of Valsalva should not exceed a temperature limit of 55°C to 60°C, a maximum power of 30 to 50 W, and energy application time of 30 to 60 seconds. Other authors recommend similar values for procedures in the aortic cusps, for example, in one center ventricular arrhythmia was ablated with a 3.5 mm open irrigated-tip catheter, targeting an impedance drop 10 to 15 ohm, with temperature limited to 45°C and power to 40 W if a coronary artery was less than 12 mm away.[58] A study of low power RF ablation carried out in the left coronary cusp with a 4 mm tip nonirrigated catheter used energy of 15 to 20 W (up to 30 W in one patient out of nine) with temperature limit of 55°C.[62] The procedure was successful in all but one patient, without recurrence during long-term follow-up. No complications were noted despite applications performed 5 to 10 mm from LMCA ostium (a Judkins left coronary catheter was kept in LMCA ostium as a marker). The authors concluded that in the view of the fact that, conversely to what was assumed earlier, VT foci are now assumed to be located in the ventricular myocardial extensions into the aorta, and not in the adjacent ventricular myocardium, low-power RF energy may be sufficient. In two patients in the present analysis, with thermal injury due to energy delivery adjacent to LMCA ostium for whom energy settings were available, the maximum energy of 30 and 40 W was used, with the temperature not exceeding 50°C. In both cases, operators assumed that safe distance of 10 mm was maintained throughout the procedure; however, irrigated-tip catheters were used, which though less thrombogenic, create deeper and wider lesions than nonirrigated systems. In future other technologies, such as high-intensity ultrasound, laser, microwave, or irreversible electroporation may prove safer than standard RF ablation.

5 | CONCLUSIONS

Although LMCA injury is an infrequent complication of catheter ablation, in patients with atypically severe chest pain, hypotension/shock, or ventricular arrhythmia nonattributable to the procedure itself, myocardial ischemia is strongly suspected, and urgent coronary angiography with rescue percutaneous angioplasty should be performed. The clinical course of LMCA dissection is usually no less dramatic than that of cardiac tamponade, therefore mandates quick diagnosis and urgent resolution for a patient to survive.

Despite the close proximity to the pulmonary artery, the anterior left atrium, the base of the left atrial appendage, and high-septal RVOT, LMCA injury has not been reported for ablation targeting these structures. Ablation-related trauma of LMCA somewhat surprisingly seems to be more often "collateral damage" of just

passing by the artery ostium than the consequence of energy application in its close proximity.

Delayed and chronic presentation of LMCA injury should be considered in patients with the history of procedures performed in LV/LVOT or the aortic cusps.

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Case Report

Delayed presentation of left main coronary artery dissection due to catheter ablation in a patient with bicuspid aortic valve. Coincidence or manifestation of inherent vulnerability?

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ABSTRACT

Left main coronary artery (LMCA) injury is an uncommon complication of catheter ablation. Due to the large myocardial area at risk, its presentation is usually acute with a dramatic course and life-threatening sequelae. Increased susceptibility to spontaneous coronary artery dissection has recently been implied in patients with bicuspid aortic valve (BAV). We present the first case of iatrogenic coronary dissection in a BAV patient, with an atypically delayed manifestation. The patient sustained ablation catheter-induced mechanical damage of LMCA due to its inadvertent penetration during the attempts to cross the aortic valve. After three days of recurring chest pain, he was readmitted with anterior myocardial infarction and imminent cardiogenic shock, and underwent emergent coronary stenting.

Literature review suggests that in BAV inherent susceptibility to both spontaneous and iatrogenic coronary dissection may exist. Therefore, we advocate that in BAV extreme caution should be exercised during electrophysiological procedures involving the coronary artery cannulation for tagging or pace mapping, or when the left ventricle is to be entered retrogradely, and likewise in percutaneous coronary interventions. Such patients may be doubly predisposed to iatrogenic injury; firstly, by more difficult catheter manipulation in the malformed aortic cusps, and secondly, by the underlying vulnerability of coronary ostia.

<**Learning objective:** Arteriopathy in bicuspid aortic valve (BAV) is not limited to the aorta. It is considered a connective tissue disease predisposing to spontaneous coronary artery dissection. This predisposition may also render the patients more vulnerable to iatrogenic dissection.

Ablation in the aortic cusps or with the aortic valve crossing, and percutaneous coronary interventions may require special precautions in the BAV population.

Physicians attending post-ablation patients should be aware of a delayed coronary artery occlusion risk.>

Introduction

Coronary artery damage is rarely observed during catheter ablation of arrhythmia. When the left main coronary artery (LMCA) and the left anterior descending coronary artery (LAD) are injured, the presentation is typically acute/subacute due to the vast myocardial territory supplied by the vessels. It usually manifests as chest pain with life-threatening ventricular arrhythmias, cardiogenic shock, or sudden cardiac arrest [1]. Prompt diagnosis and urgent treatment are required to save the patient.

Recent studies suggest that bicuspid aortic valve (BAV) is a condition predisposing to spontaneous coronary artery dissection [2]. The underlying susceptibility to spontaneous dissection may also render coronary arteries more vulnerable to catheter-induced injury.

With BAV being the most prevalent congenital heart disease (estimated incidence of 1-2%) and the constantly growing number of transaortic electrophysiological procedures and percutaneous coronary interventions, a substantial population may be at inherently increased risk of iatrogenic coronary dissection.

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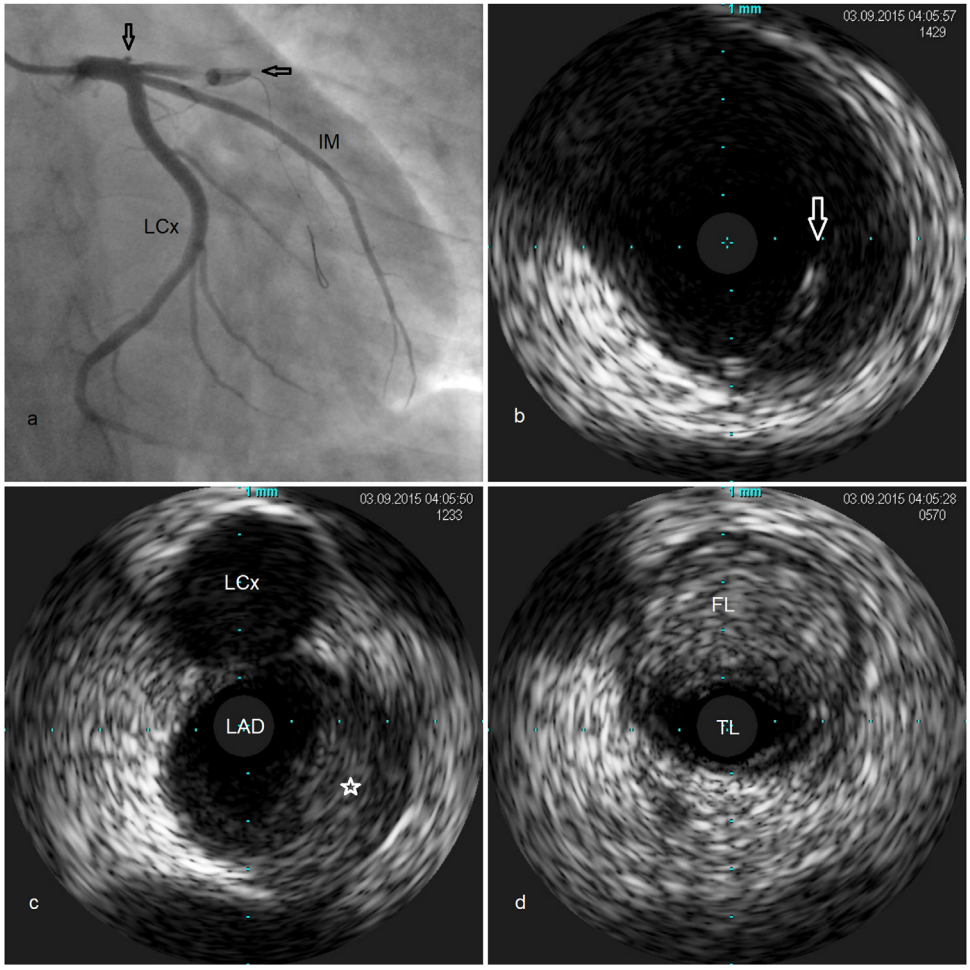

Fig. 1. (a) Angiographic image (LAO 7° CAUD 30°) of the left anterior descending artery (LAD) proximal occlusion (horizontal arrow) with a pinhead-shaped extraluminal dye penetration just before the vessel origin (vertical arrow) as a presumed site of the ablation catheter impact. IM, intermediate branch; LCx, left circumflex artery (guiding catheter: EBU 3.5 6 French). (b) Intravascular ultrasound image of the dissection entry site in the left main coronary artery (LMCA), with an intimal flap (arrow). (c) LMCA bifurcation with the intramural hematoma (asterisk) in LAD and the uncompromised LCx. (d) Mid-LAD with the collapsed true lumen (TL) compressed by the thrombosed false lumen (FL).

Case report

A 27-year-old man was admitted to our department due to recurrent chest pain with concomitant weakness and vomiting. In the electrocardiogram (ECG), sinus tachycardia with ST segment elevation in anterior precordial leads was found. His blood pressure was 80/50 mmHg and required dopamine infusion. In echocardiography, the ejection fraction was 30–35%, with akinetic interventricular septum and all apical segments, and hypokinetic anterior wall. High-sensitivity troponin T on admission was 6.34 (upper limit of normal: 0.014). Acute myocardial infarction with imminent cardiogenic shock was diagnosed. His medical history included BAV, subarachnoid hemorrhage, Wolff-Parkinson-White syndrome with two attempts of transseptal radiofrequency (RF) ablation (4 and 7 months before admission), and transaortic redo ablation performed 3 days earlier at a tertiary center.

We proceeded with urgent coronary angiography, in which LAD occlusion was found with haziness in its proximal segment, and an extraluminal, round-shaped penetration of dye at the LMCA bifurcation (Fig. 1a, Online Videos 1, 2 in Supplementary material). The left circumflex artery (LCx) and a large intermediate branch (IM) were without obstruction. Intravascular ultrasound (IVUS) examination was performed to confirm and assess the extent of the suspected coronary dissection. The dissection entry site with a moving flap was found at the LMCA bifurcation (Fig. 1b, Online Video 3 in Supplementary material). The dissection extended down to the 1st diagonal branch origin. In IVUS, the collapsed true lumen of LAD with thrombosis of the false lumen was seen (Fig. 2c–d, Online Video 3 in Supplementary material). Fortunately, the dissection did not propagate retrogradely into the aortic root and the ascending aorta, as confirmed later by transesophageal echocardiography.

Due to LMCA large diameter (6 mm), a self-expanding stent Stentys 3.5–4.5/25 mm (Stentys SA, Paris, France) was implanted from LMCA into LAD. The distal part of the dissection was covered with an overlapping drug-eluting stent. Thrombolysis in myocardial infarction 3 flow was achieved, yet with poor myocardial blush (Fig. 2a, Online Video 4 in Supplementary material). LCx and IM ostia were not compromised by the stent. The latter and the adequate stents' apposition were checked in IVUS (Fig. 2b, Online Video 5 in Supplementary material).

As reported by the electrophysiologist, the left posterolateral accessory pathway had been ablated by retrograde approach, with RF applications performed in the left ventricle near the mitral valve annulus. The EnSite cardiac mapping system (St. Jude Medical, St. Paul, MN, USA) had been utilized. In the preprocedural echocardi-

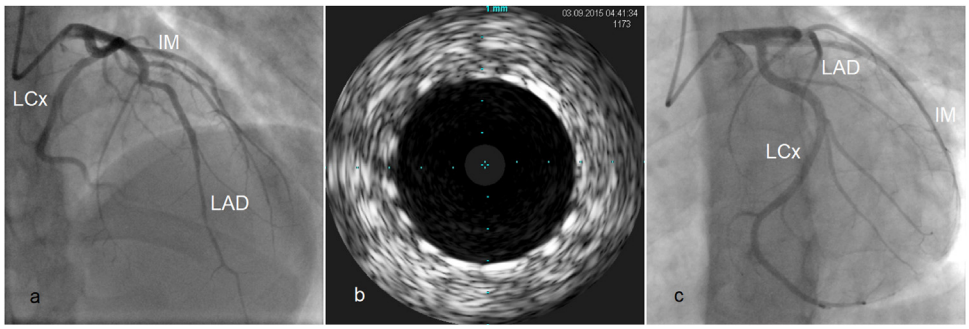

Fig. 2. (a) Angiographic image (LAO 0° CRAN 40°) of the final result after stents deployment; IM, the intermediate branch; LAD, left anterior descending artery; LCx, left circumflex artery. (b) Intravascular ultrasound image of self-expanding stent apposition in the 6-mm-wide left main coronary artery. (c) 3-month control angiography (LAO 27 °CAUD 20°) showing stents' patency and the unobstructed LCx and IM ostia.

ography, the aortic root dilatation and valve stenosis were not found (only mild regurgitation) (Fig. 3a, Online Video 6 in Supplementary material). According to the operator, significant difficulties had been encountered while crossing the aortic valve, requiring extensive manipulation, and thus inadvertent LMCA penetration during 7 French Thermocool catheter introduction could be assumed post hoc. However, catheter insertion into LMCA had not been suspected during the procedure. LMCA had not been intentionally entered to tag its position on an electroanatomical map. The catheter position in the left ventricle had been stable and dislodgement into the aorta during energy application had been ruled out. After the procedure, the patient had complained of persistent chest pain. Due to ECG changes (minor ST-segment elevation in leads V4-V6), echocardiographic examination had been performed but had shown normal contractility and no pericardial effusion. In ECG, preexcitation had recurred on the following day.

After stenting, the patient recovered and was discharged eight days later. Repeat angiography after 3 months confirmed stents' patency in LMCA-LAD and unobstructed LCx (Fig. 2c, Online Video 7 in Supplementary material). The patient declined implantable cardioverter-defibrillator (ICD). One year later, he was resuscitated due to ventricular fibrillation. In angiography, a good long-term result of LMCA-LAD stenting was found. ICD was eventually implanted. One month later, another episode of ventricular fibrillation occurred with adequate ICD intervention. The patient has been suffering from exertional dyspnea since the infarction.

Discussion

Along with cardiac tamponade and atrioesophageal fistula, coronary artery injury is among the most dire and potentially lethal complications of catheter ablation. In cases of LMCA trauma with acute/subacute presentation, in-hospital mortality has been assessed as 32% [1]. Due to the large area of myocardium at risk, LMCA and LAD injury causing flow deterioration typically manifests during an ablation procedure or shortly after its termination. The unusually late presentation in our patient may have been the result of gradual propagation and thrombosis of intramural hematoma after the intraprocedural LMCA bifurcation's spot damage. Seven French ablation catheter would have been easily accommodated by the 6-mm LMCA of our patient. The extraluminal cap of dye visible just before LAD origin had most likely been the impact site. As observed during complicated by dissection coronary interventions and retrograde ablation procedures, the cranial surface of LMCA is the place of catheter tip impact, as catheters are naturally pointed in this direction by their curves and the aortic cusp backup [1]. In a retrospective analysis of 26 cases of LMCA injury during ablation, unintended catheter insertion was inferred in 73%, with 95% of the latter having involved the aortic valve crossing (only in 18% LMCA penetration had been realized before symptoms/ECG changes developed) [1]. Moreover, spontaneous coronary artery dissections (SCAD) predominantly affect mid-to-distal segments [2]. Although we cannot unequivocally exclude stress-induced spontaneous dissection in this patient, the course of events, high proximal location of

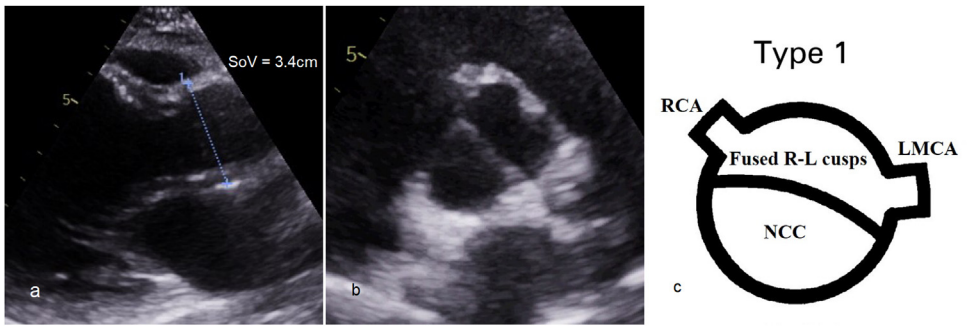

Fig. 3. (a) Transthoracic echocardiography of the aortic root in parasternal long-axis view with width measurement at the sinuses of Valsalva (SoV) level. (b) Parasternal short-axis echocardiographic view in diastole, showing the patient's bicuspid aortic valve (BAV) with nearly equal cusp size and right-left orientation of the commissure. BAV type 1, i.e. with fused right and left coronary cusps without raphe can be seen. (c) Schematic representation of type 1 rapheless BAV. LMCA, left main coronary artery; NCC, non-coronary cusp; RCA, right coronary artery.

dissection entry, and the extraluminal outpouching strongly suggest iatrogenic etiology.

The delayed presentation raises some important issues. Patients after electrophysiological procedures usually stay overnight in hospital with next-day discharge, as was the case in our patient. Chest pain or discomfort are typical complaints after ablation procedures and are not specific to ischemia in this population. In patients with ablation performed near a coronary artery ostium or its anatomic course, prolonged monitoring and follow-up with a low threshold for ischemia diagnostic tests should be considered.

Another important aspect of our case is the coincidence of BAV and iatrogenic coronary artery dissection. BAV is regarded as a heritable disorder of connective tissue and is associated with cystic medial degeneration that can lead to the progressive dilation of the aortic root as well as aneurysm and dissection of the ascending aorta. Arteriopathy in BAV is not limited to the aorta; intracranial aneurysms and spontaneous dissections of the cervical and intracranial arteries have been described in this population [3]. During retrograde electrophysiological studies, LMCA is sometimes intentionally entered to mark and tag its location on a three-dimensional electroanatomical map, or to perform pace-mapping. Even with its inadvertent and uncontrolled penetration, LMCA damage is not an inevitable consequence, particularly in young patients without atherosclerotic lesions. However, a malformed bicuspid aortic valve may prove more difficult to cross, increasing the risk of forceful LMCA intubation with a rather stiff ablation catheter. Moreover, recent studies suggest that coronary arteries may be more dissection-prone in patients with BAV. In the 2018 American Heart Association statement on SCAD, BAV was included in the screening list among other connective tissue disorders such as Marfan and Ehlers-Danlos syndrome, association of which with SCAD is well established [2]. However, only few cases of SCAD afflicting patients with BAV have been published so far [4–6]. As recently found, patients with SCAD, admittedly a heterogenous group, have also >17-fold higher incidence of catheter-induced coronary artery dissections [7].

As mentioned by Andreou, there may exist a common underlying defect in patients with BAV, as the aortic cusps, musculoconnective tissue of the ascending aorta, and the aortic arch all derive from the neural crest cells (NCCs), whose malfunction is a proposed pathogenetic factor in the most prevalent BAV type 1, i.e. with fused right and left coronary leaflets (found in our patient) (Fig. 3b, c) [8,9]. The NCCs also directly contribute to the formation of vascular smooth muscle cells of the ostial regions of coronary arteries and play a regulatory role in the whole coronary artery development, with some coronary variants and anomalies more prevalent in BAV populations [2,10].

Patients with BAV may thus be doubly predisposed to iatrogenic coronary artery injury: firstly, by more difficult catheter manipulation in the malformed aortic cusps with their distorted geometry, and secondly, by the inherent susceptibility to coronary dissection. As BAV is the most prevalent congenital heart disease, our observation suggests that during electrophysiological procedures requiring the aortic valve crossing, or performed near the coronary ostia, and in percutaneous coronary interventions, particular caution should be employed to prevent potentially fatal complications.

The reported case should also warn physicians attending post-ablation patients of the risk of a delayed coronary artery occlusion. In patients with recurring or protracted chest pain, prolonged monitoring and repeated check-up should be mandatory after procedures with an increased risk of a major coronary artery damage.

Conflict of interest statement

The authors declare that there is no conflict of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jccase.2020.07.004.

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