REPUBLIC OF TURKEY
ACIBADEM MEHMET ALİ AYDINLAR UNIVERSITY
INSTITUTE OF HEALTH SCIENCES

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AHMET KARABULUT

DOCTORATE THESIS

DEPARTMENT of MEDICAL BIOTECHNOLOGY

SUPERVISOR
Prof. Dr. Zühtü Tanıl Kocagöz

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DECLARATION

I hereby declare that, this thesis is my own work and it has been written by me. All the information in this thesis was obtained within the academic and ethical rules. No part of this work has been previously presented in a meetings or published in a journal. There is no conflict of interest regarding this thesis. I state that I have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved. The individual information about each cases did not expressed in the dataanalysis. There is no financial relationship with a company and this work was not supported by any company.

05.01.2021

Ahmet Karabulut

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‘’Education is a life-long activity. Learn it, experience it and share it’’

This motto encouraged me to start this doctorate program which widen my horizon over the medical diagnosis and treatment. In this valuable page, I would like to send my special thanks to people who had an impression on my doctorate program.

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LIST OF ABBREVIATIONS AND SYMBOLS

BMI: Body mass index

CA: California

CABG: Coronary artery bypass graft

CCS: Canadian Cardiovascular Society

CI: Confidence interval

CT: Computed tomography

CTO: Chronic total occlusion

DM: Diabetes mellitus

E-CTO: Euro chronic total occlusion

F: French

GFR: Glomerular filtration rate

gr: Gram

HT: Hypertension

IVUS: Intravascular ultrasonography

J-CTO: Japan registry of chronic total occlusion

kg: Kilogram

LAD: Left anterior descending artery

LCX: Left circumflex artery

LVEF: Left ventricular ejection fraction

MA: Massachusetts

MDRD: Modification of Diet in Renal Disease Study

MI: Myocardial infarction

mg/dl: Miligram/deciliter

ml: Mililiter

mm: Milimeter

PCI: Percutanous coronary intervention

PTFE: Polytetrafluoroethylene

RCA: Right coronary artery

TIMI: Thrombolysis in myocardial infarction

USA: United States of America

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SUMMARY

Procedures for the chronic total occlusion (CTO) is a still clinical challenge with relatively lower success rate. Recent advance in the biotechnology and introduction of CTO dedicated guidewires increased the procedural success rate of CTO interventions. Herein, we aimed to reveal the preference and success rate of 0.014 inch (0.36 mm) coronary guidewires in the CTO interventions. A total of 177 patients with indication of coronary CTO procedure were included to study. Use of 1-3 guidewires and crossing of the CTO lesion with initial choice guidewires was defined as rational guidewires usage. The CTO lesions was classified according to J-CTO score and Eurocto score for evaluating the difficulty of the procedures. Then statistical analysis was performed to assess the guidewire choise, crossability and contributors of rational guidewire usage. The mean J-CTO score was 1.42±1.16 and the mean Eurocto score was 1.44±1.18. Success rate of the procedures was 90,4%. Initial choice guidewires was crossed the lesion in the 44,1 % of the cases in which 1-3 guidewires was used (82,1%). Crossability of polymeric and moderate tip stiff guidewires are higher (82,1% and 64,1%) and Pilot series was the most successfull brand (36,2%). Logistic regression analysis confirmed that J-CTO score, procedural technique, guidewire type and the tip stiffness was the major predictors of rational guidewire usage. Our analysis showed that, use of polymeric and moderate tip stiff guidewires, particulary Pilot brand, is associated with economical and rational guidewire usage in the easy and intermediate difficulty CTO cases.

Keywords: Atherosclerosis, Biomaterials, Coronary chronic total occlusion, Guidewires, Percutanous coronary intervention

ÖZET

Koroner kronik total oklüzyon girişimlerinde 0.014 inç kılavuz tel seçimi ve kılavuz tellerin başarı oranı

Kronik total oklüzyon (KTO) girişimleri zorlu işlemler olup, göreceli olarak düşük başarı oranına sahiptir. Biyoteknolojideki gelişmeler ve KTO girişimlerine özel kılavuz tellerin üretilmesi, işlemlerdeki başarı oranını arttırmıştır. Bu araştırmada, işlemlerde tercih edilen 0,014 inç (0,36 mm) kılavuz tellerin başarı oranını saptamayı amaçladık. Toplam 177 KTO işlemi uygulanacak hasta çalışmaya dahil edildi. Toplamda 1-3 kılavuz tel kullanılması ve KTO lezyonunun ilk seçilen kılavuz tel ile geçilmesi rasyonel kılavuz tel kullanımı olarak tanımlandı. Lezyonların zorluk derecesini ölçmek için J-CTO ve Eurocto skorlarına göre sınıflama yapıldı. Sonrasında kılavuz tel seçimi, kılavuz telelrin lezyonu geçiş başarısı ve rasyonel kılavuz tel kullanımının öngördürücülerini saptamak için istatistiksel analiz yapıldı. Ortalama J-CTO skoru 1.42±1.16 ve ortalama Eurocto skoru1,44±1,18 olarak saptandı. İşlemlerdeki başarı oranı %90,4 olarak izlendi. Vakaların %44,1'inde ilk seçilen kılavuz tel ile lezyon geçildi ve bu işlemlerde çoğunlukla 1-3 adet kılavuz tel kullanıldı (% 82,1). Polimerik ve orta değerde uç ağırlığına sahip kılavuz tellerin lezyon geçişi daha iyiydi (%82,1% ve % 64,1). Pilot serisi % 36,2' lik oranla lezyon geçişinde en başarılı kılavuz tel grubu oldu. Lojistik regresyon analizinde, J-CTO skoru, işlem tekniği, kılavuz tel tipi ve uç ağırlığı rasyonel kılavuz tel kullanımın ana öngördürücüleri oldu. Kılavuz tel olarak polimerik yapılı, orta değerde uç ağırlığına sahip kılavuz tellerin, özellikle de Pilot grubu kılavuz tellerin tercih edilmesi, basit ve orta zorluktaki KTO girişimlerinde ekonomik ve rasyonel kılavuz tel kullanımı ile ilşkilidir.

Anahtar Sözcükler: Ateroskleroz, Biyomateryal, Koroner kronik total oklüzyon, Kılavuz tel, Perkütan koroner girişim

1.BACKGROUND AND AIM OF THE STUDY

Atherosclerosis is defined as the accumulation of the fatty and fibrous material in the intimal layer of the arteries. Atherosclerosis is a leading cause of morbidity and mortality in all over the world. One third of the all deaths occur secondary to arteriosclerosis and complication of atherosclerosis (1). Involvement of the coronary vessels would lead to acute coronary syndromes and myocardial infarction which is a major killer in the worlwide. Involvement of the aorta, carotid vessels would lead to transient ischemic attack and stroke which constitude the leading cause of disability and mortality (1). Involvement of the peripheral vessels in the upper and lower extremity would lead to claudication, ulceration and amputation. Moreover, involvement of the visceral vessels would lead to others important clinical syndromes.

Progressive arteriosclerosis of the coronary vessels would lead to coronary occlusion which is the major indication for the percutanous coronary interventions. Acute occlusion of the coronary vessels are usually presentedas a acute myocardial infarction. Immediate therapy of such lesion is crucial for prevention of mortality and morbidity (2). Contrary to, acute occlusion, asymptomatic stenosis and occlusion of the coronary vessels may occur as a result of progressive atherosclerotic process. In such scenario, patient could be defitively free of the clinical symptoms even coronary vessels was totally occluded. Special clinical test could be performed to show ischemia in the myocardial tissue. Gold standart for the diagnosis of coronary artery disease is coronary angiography. Significance of the coronary arteries occlusion could be identified with coronary angiography and definitive treatment would be scheduled according to angiographic images (2).

Biomaterials are the cornerstones in the diagnosis and treatment of the coronary artery disease. For the diagnostic angiography, canules, catheters and guidewires are the standart equipments (3). However, more sophisticated biomaterials are usually used in the treatment of coronary stenosis and occlusion. Balloon angioplasty and stent deployment is the well accepted methods for the treatment of coronary occlusion (2). Special catheters and guidewires could be preferred according to characteristic of the coronary lesions (3). The overall success rate is over the 95 % for most of the percutaneous coronary interventions.

Coronary chronic total occlusion (CTO) is a challenging clinical scenario in the percutaneous interventions. Coronary occlusion more than 3 months defined as a chronic total occlusion. With the conventional percutanous coronary intervention (PCI) strategy, the success rate of CTO interventions are relatively lower comparing to standard coronary lesions (4). The success rate could be lower as 50 % especially in the older lesions which previously operated. Biomaterials play a critical role for the recanalization of CTO lesion. All the CTO procedures are usually performed with 0.014 inch (0.36 mm) guidewires and crossing of the total segment with such guidewines is a major step for the successfull procedure. Soft, non-hydrophilic 0.014 inch coronary guidewires are usually enough to treat standard coronary lesions. However, special guidewires with different features were brought into use to increase the success rate of more complex interventions (5). Although, newly introduced guidewires are more smart and facilitating the guidewire penetration, their clinical usage usually variate according to operators and clinical centers. Higher cost and operator's routine practice are the major determinants of guidewire preference. Guidelines and the expert opinions are also important in the preference of coronary guidewires.

1.1.Aim of the thesis

Herein, we aimed to investigate preference and success rate of coronary guidewires in the chronic total occlusion interventions. Multiple 0.014 inch guidewires are usually necessary to perform CTO interventions. After detailed analysis of the guidewires usage, we are planning to define an algorithm for coronary guidewire preference according to lesion characteristics and guidewire success. We also going to focus on the rational guidewire usage and crossability of the guidewires. We will discuss the clinical and angiographic determinants of the crossing ability of the initial choice guidewire and their clinical implications. We will also assess the use of new release biotechnologic guidewires in the CTO procedures.

2.INTRODUCTION

Medical biotechnology and innovations have a notable influence on the CTO interventions. In last two decades, parallel to innovations in the medical biotechnology, CTO interventions were become more popular. With the use of dedicated instruments, the success rate of CTO interventions were reached to an amazing ratio. In this section, initially we will define the CTO lesion and then we will talk about the correlation between biotechnology and CTO procedures. Finally, we briefly summarized the composition of major 0.014 inch guidewires used for CTO interventions.

2.1.Chronic total coronary occlusion

Coronary chronic total occlusions are described as an occluded coronary artery with thrombolysis in myocardial infarction (TIMI) flow 0 for a period exceeding 3 months (4). Chronic total occlusions are one of the most challenging targets of percutaneous coronary intervention (PCI). Comparing to non-CTO PCI, the procedural success rate is lower and it has greater complication rates, more radiation exposure and longer procedural times due to its complexity (6).

Complete coronary revascularization is a crucial strategy in the multivessel coronary artery disease. Presence of CTO was the strongest independent predictor of incomplete PCI in the multivessel diseases which associated with worse prognosis (6). Presence of CTO lesion is an usual indication of coronary bypass surgery. However, occlusion of the bypass graft would necessitate the CTO interventions since totaly occluded bypass graft was untouchable due to higher perforation risk.

Untreated CTO lesions have a important impact on the prognosis of the patients. Anginal attacks and arrythmia is more common with CTO lesions. Long-term follows showed that CTO lesions are associated with decreament in the left ventricular ejection fraction and heart failure devolepment which is an omnious prognostic factor for the future follows. So we can proposed that, presence of CTO lesion is associated with shorter life span.

In addition, coronary artery bypass graft (CABG) surgery may serve as a temporary solution. The patency rate of the bypass graft could be as lower as 50% within the 10 year follow-up (7). Patency rate is extremely lower for venous graft and graft failure even in the first post-operative year is not rare condition. Early bypass graft failure is a significant problem especially in the young patients. Second bypass surgery is associated with higher mortality and morbidity which enforce physician to medical treatment. Relieves of the anginal symptoms with medical therapy could be very difficult in certain cases. Percutanous CTO interventions are the only resort for such a symptomatic patients.

In the standard coronary procedure, simply guiding catheter, 0.014 inch guidewire, balloon catheter and stents are the necessary biomaterials for the procedure. In the most cases, conventional soft floppy guidewire is enough to perform the procedure.

On contrary, these instruments usually not capable to perform a successfull CTO interventions. From these point, a several biotechnology company focused on to develop CTO specific instruments includings microcatheters, balloon catheters and guidewires. The cornerstone maneuvers in the CTO interventions is penetration of CTO segment with the 0.014 inch guidewires (8). This step is crucial for the successfull CTO interventions and this step mainly dependant to guidewire choice. Biotechnologic innovations lead to introduction of a lot of dedicated guidewires for CTO interventions (9). Although, there is a variety of dedicated guidewire, their clinical use is variable and the number of commonly preferred CTO guidewires are roughly ten. Asahi Intecc, Abbot Vascular, Boston Scientific are the leading companies that manufacturate CTO dedicated guidewires. The higher cost of these guidewires are one of the major limitation of their clinical usage. The total cost of the CTO interventions is roughly 10-20 times higher than standard procedure. Multiple guidewire use would increase the total cost which would be an important issue for the patients.

Guidewire choice should be done according to lesion characteristics (9). The operators also should be familiar with the composition and behaviours of the CTO guidewires. Penetration of the CTO segment with the first choice guidewire would be excellent for the procedural time, complication rate and total cost. Prior to CTO procedure, extensive analysis of the CTO segment is very important. Proximal and distal occlusion cap, length of the lesion, calcification, bending, presence of collateral circulation, presence of micro-channel, landing zone, catheter back-up are all important feautures for guidewire selection (10). The new generation guidewires have a very complex design (11). The operators should know the the composition of each CTO guidewires and their characteristic behaviours within the vessel lumen and CTO segment.

2.2.Medical biotechnology in CTO interventions

Medical biotechnology play a central role for the innovation in the CTO procedures. Biomaterials are the essentials elements of CTO interventions. Biomataterials are first described by the Williams in 1987. A biomaterial is a nonviable material used in a medical device, intended to interact with biological systems. This interaction could be temporary or permanent according to procedure. There is a temporary interaction between the guidewires and CTO lesion which resulted with stent implantation in successfull procedure. In addition to biocompatibility, the guidewires should advance through the lesion without any serious complication. CTO guidewires have a excellent biocompability. The tendency for thrombus formation is well-known undesirable effects of all guidewires which solved by the effective heparin administration during the procedure. The other hazardous result like dissection, perforation or jail of the guidewire mainly depend on the operators experience and maneuvers. The major biomaterials used in CTO interventions are guiding catheters, 0.014 inch dedicated guidewires, balloon catheters and stents for final step (11).

2.2.1.Composition of Coronary Guidewires

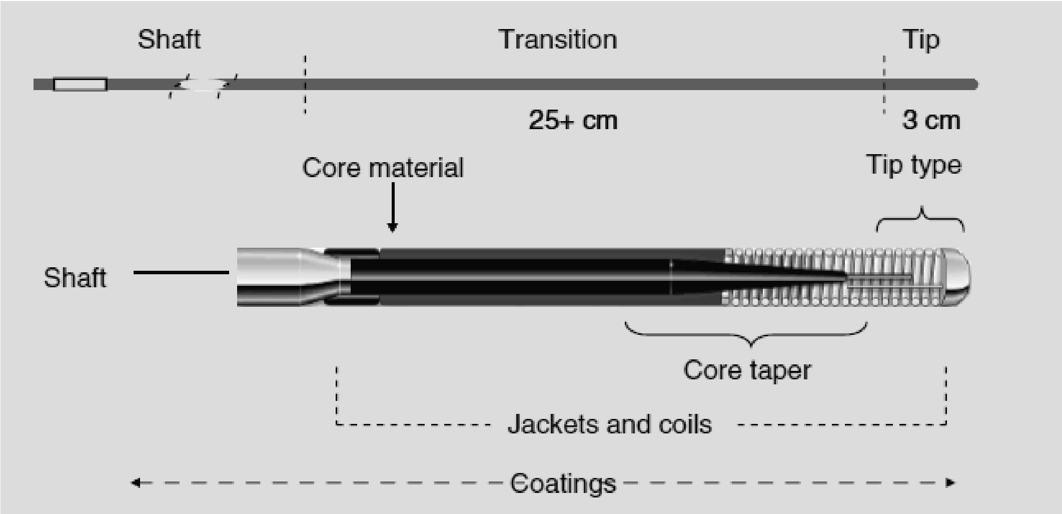
Coronary guidewires are the most important biomaterials for the successfull procedure. They provide the primary interface between the hands of the operator and the CTO segment. No other piece of PCI equipment directly influences the progress of the CTO procedure. The guidewires could be described as a hands of the operator. They should transmit all the maneuvers of the hands to CTO segment.

Each coronary guidewires have shaft (body), transition zone, tip, core material, jacket and coating components (5) (Figure 1).

2.2.1.1.Shaft

The guidewires shaft usually accepted as a least critical portion of the guidewire component. The shafts are most commonly constructed of solid high-tensile stainless steel of cross-section and measuring slightly less than 0.014 inches in diameter. Nitinol alloy also less commonly used for the shaft generation. Composition of the shaft is important for kink resistance, torque transmission and column strength (5).

Shaft portion of the guidewires usually supported by the second biomaterials, microcatheters, which enhance the column strength and torque transmission (10).Core and tip of the guidewires are more important comparing to shaft portion. Mostof the biotechnologic investigations was performed on the core and tips of the guidewires which yielded to introducing of the new smart guidewires with different structure (11).



This image is taken from the Interventional Cardiology (ISSN:1755-5310 e), 2013:5(5) issue for the demonstration of the product.

Figure 1. Basic structure of 0.014 inch coronary guidewires.

2.2.1.2.Core

It forms a transition zone between shaft and tip of the guidewire. It is a stiffest part of the guidewire which provide stability and steerability (5). Core material affects the flexibility, support, steering and trackability. New generation CTO guidewires usually have more complex core structure comparing to conventional guidewires (12). The core portion transmit longitudinal and rotational forces from the shaft to tip region. Core segment should also track and conform to the tortuosity inherent in guiding catheter tips and arteries. Core segment is bonded, welded or structurally continous with the distal border of the shaft portion. Core is usually more flexible thand shaft through a reduction in its diameter or by use of more flexible alloys.

Distal segment of the core is usually tapered to increase the flexibility of the tip segment. Cores are usually 25-30 cm in length, manufactured from stainless steel or formed from super elastic nitinol (a nickel-titanium alloy). Stainless cores are easy to weld and machine, tend to optimize torque transmission, and also offer a greater support fo the delivery of the over the wire devices. It provides good shapeability and can deliver more push for penetration. But they are less flexible and susceptible to kinking. Nitinol cores offer more flexibility and their structure is predominantly kink resistant.They are pliable but supportive. They tend to return their original shape which making them resistance to deformation in prolonged use. Hovewer, their torquability is lower than stainless steel. Kink and fracture of the core portion of the guidewires are the major problem treating the tough and tortuos lesion which lead to use of multiple guidewires. Core diameter influences the performance of the wire. Larger diameter improves support and allow 1:1 torque transmission. Smaller diameter enhances flexibility.

Distal tapering usually produced by grinding (Figure 2). Step-wise tapering is easy to manufacture, whereas, it produces mechanical discontinuities that may lead to prolapse, kinking or rupture of the distal portion. Conical and parabolic grinds usually performed as a newer design to reduce such kind of complications. There is a inverse relationship between grinds that optimize flexibility versus support (Figure 2). Long taper and larger number of segmented tapering increases the flexibility. Short taper and smaller number of wide spaces gradual taper increases support and transmission of push force. Thus, shorter taper means less trackability, more support, more prolapse tendency. Whereas, longer taper means more trackability, less rail support, less prolapse tendency. Extra-support wires carry the full diameter of their stainless steel cores more distally compared with standard wires. This property is helpfull especially in tortuous lesion.Single core wires are superior in force transmission.

2.2.1.3.Tips

The distal 3 cm of the guidewires generally described as tip portion (5). This segment directly face with intraluminal lesion and it plays a critical role in determining the performance characteristics perceived by operators (13). Steerability and softness of the tips portion are important features for optimal movement of guidewires. The structure of tip can be variable. One piece core tapered in which tapered core reach distal tip. It offers beter force transmission to tip and greater tactile response for operators. In two piece core, distal core does not reach to distal tip of the wire. Shaping ribbon was the basic structure of the distal tip. Two piece tip offers easy shaping and durable shape memory (Figure 3).

The end of the wire tip is wrapped in a ribbon of flexible metal to make the tips more flexible and atraumatic. On nitinol wires, the shaping ribbon is required to help retain the shape of the tip. The design of the coils helps determine a wire's torque and crossability (14). The use of spring coils can provide more tactile feedback to the operator, but these tips increase the amount of friction, making them more difficult to navigate in tortuous vessels (Figure 4). One recent innovation in tip technology was a micro-cut nitinol sleeve that replaced the coiled metal tip.

The prototype of first generation steerable wire is Hi-Torque Floopy (Advanced Cardiovascular System, CA,USA). Contrary to conventional core-to-tip design, they terminated the solid core several centimeters from the wire tip and replacing it with a thin, flat stainless steel shaping ribbon (4). This new design offer softer and safer wire tips. A stainless steel coils placed over the tapered core which influences flexibility, steering, support, tracking, visibility and tactile feedback. Platinum coils also can beused alternate to stainless steel (Figure 4). A platinum wire wound in a tight helix to cover the shaping ribbon which defined as spring-coil tip design. This new feature provided rotational axis rigidity, dense radiopacity and a surface for bonding the tip components (15). Development in the design of the guidewire tips creates a new description, tactile feedback of the wire tips. It allowed operators to feel interaction between the wire and the endoluminal surface of the vessel and the lesion.

Although the shaping ribbon design guidewire tip enhance the steerability of guidewires, their penetration power is relatively low and rate of bending and fracture of the tips were common. Thus, biotechnoloy worked on the core-to-tip design also to produce wires with greater tip loads (4). Combined with a helical wind, core-to-tip design allows engineers to create tips with specific loads governed by the material and grind profile of the tips to reduce tip diameter below the 0.014 inch.

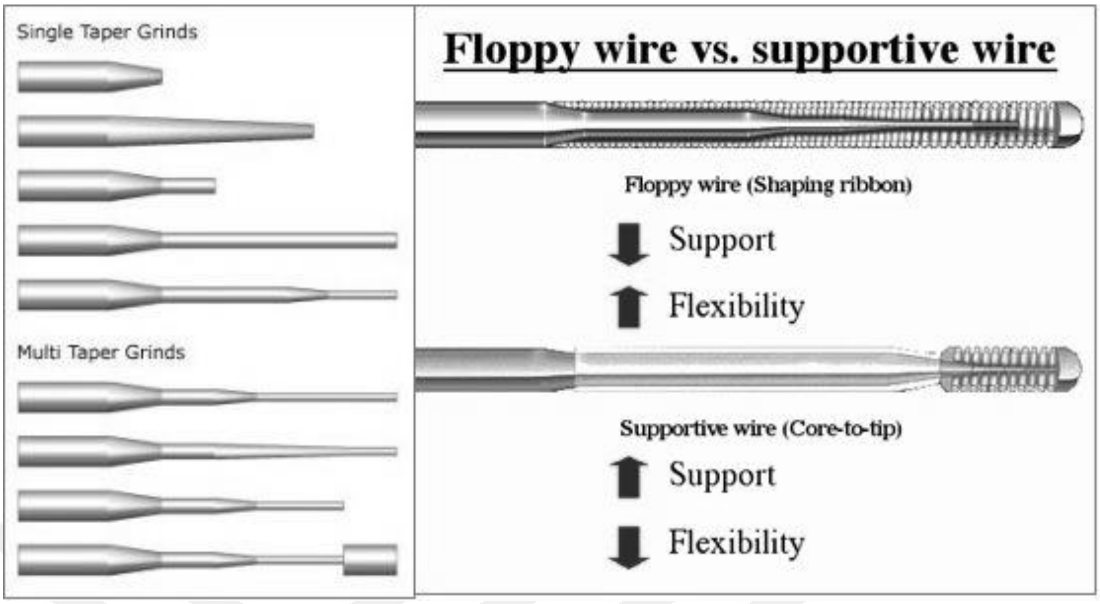


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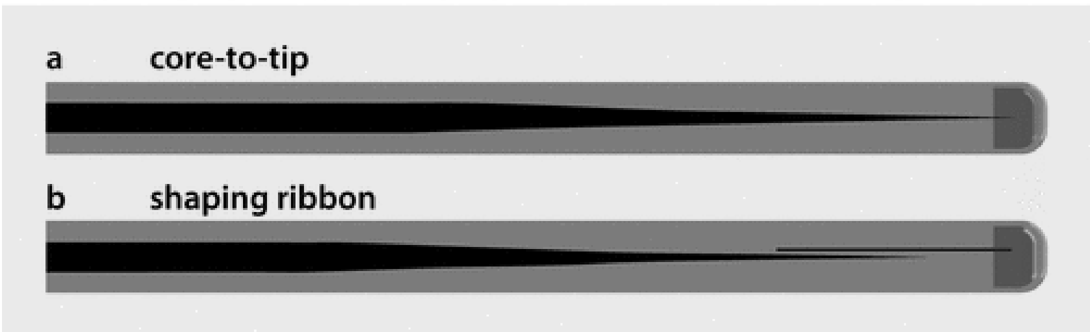
Figure 2. Different type of guidewire tapering composition and their effect on the support and flexibility.



This image is taken from Toth GG et al. Heart 2015;101:645–652 for the demostration of the product.

Figure 3. Basic composition of guidewire tips.

This image is taken from the official site of Boston Scientific and Asahi Intecc for the demostration of the product.

Figure 4. Tip structure of the guidewire with different composition.

Two newer core-to-tip design was introduced by Boston Scientific and Asahi Intecc recently (15-16). The kinetic design employes a micro-machined matrix to optimize the balance between rotational and translational rigidity with a single element that can be made to vary over its length. Compound core designs have been introduced by in the Sion line of guidewires (15). Sion wires employ double spring coil winds over solid and twisted core elements to increase rotational rigidity while maintaining extremely low bend stiffness. We are going to briefly summarize the Sion guidewires in the future section.

2.2.1.4.Polymer

Many guidewires employ a poylmer component over the core and tip portion of the wires (5). The prototype of the polymer wire is Choice PT manufactured by Boston Scientific (16). Herein, a polymer element covers a tapered transitional core creating a true polymer-only wire tip which provide more slippery tips. Contemporary polymer wires (Fielder wires by Asahi Intecc, Nagoya, Japan; Pilot wires by Abbott Vascular, CA, USA) employ a jacket or sleeve of polymer fitted over a conventional spring-coil core-to-tip chassis to enhance wire shaping, torquecontrol and steering (15,17). Generally, proprietary variant of polyurethane used for polymer jackets. In combination with hydrophilic coatings, there would be marked reduces friction between the wire and wet or water-containing surfaces and tissues. However, this new design may limit the shape retention and torque control. In addition, abrasive surfaces (severe calcification at bends, stent struts, high pressure stent jailing) may score or even strip the polymer which lead to retension of the foreign material (18).

2.2.1.5.Hydrophilic or hydrophobic coating

Wires can be coated in polymers to make them more hydrophilic or hydrophobic (5). Hydrophobic coatings are usually made of silicone and repel water to reduce friction, increase trackability and offer good tactile feedback. Hydrophilic coatings attract water and the coating becomes a gel when wet. This makes the wires more slippery and reduces friction, helping increase trackability. However, hydrophilic wires are not recommended as a first choice because the slippery tip can slide between plaque and create a dissection during insertion. These wires also can cause perforation and because they have less tactile feedback for tissue resistance.

Nearly all contemporary coronary guidewires have a thin coating applied as the final manufacturing step. Some wires employ both but at different positions along the wire length. Hydrophilic coatings (e.g, polyethylene oxide or polyvinyl pyrolidone) require water activation to become slippery, but once wet have extremely low coefficients of friction (13). When used inside very tight-fitting catheters, the boundary layer of water can be excluded, leading to paradoxic sticking and locking. Hydrophobic coatings (i.e, polytetrafluoroethylene or silicones) are inherently slippery and do not require water for activation. Silicone or its variants are commonly applied to wire shafts to improve movement through plastic catheters. Both hydrophilic and hydrophobic coatings may chafe or degrade with use. This can account for the degradation in wire performance sometimes noted during long procedures, particularly when wires are working through areas of severe tortuosity and friction. Non-coated hydrophobic wires have better tactile response and good trackability. Asahi soft guidewire and Boston Choice Floppyare the example of widely used hydrophobic guidewires. Hydrophilic wires have better trackability and lesser friction. Whereas, tatctile response is not good and intense push may lead to perforation. Boston PT floppy is a example of widely used hydrophilic guidewire.

2.2.2.The major behaviorial characteristic of the guidewires

2.2.2.1.Torqueability

It is an ability to apply rotational force at a proximal end of guidewire and have that force transmitted efficiently to achieve proper control at the distal guidewire tip (12).It can also described as 1:1 transmission of the bend. Tensile strength of the core material, shear modulus and wire diameter are important factors for torqueability.Stainless steel core has a better torqueability comparing to nitinol core materials.Guidewires with novel technology of dual or composite core composition have a superior torqueability.

2.2.2.2.Trackability

It is an ability of wire to follow the wire tip around curves and bends without buckling or kinking, to navigate anatomy of the vaculature (12). Gradual or long tapered tips provide superior trackability.Less stiff, floppy wires can navigate sharp bends much easier than stiff wires. Trackability is usually determined by the lateral support provided by the guidewire. Trackability is affected by how the tip is designed and the material of the core wire.

2.2.2.3.Steerability

It is an ability and responsiveness of a guidewire tip tonavigate vessels and to be delivered to desired position within the vessel (12). This feature is especially important in drilling strategy where wire is rotated in a controlled manner. Core to tip design provide superior steerability and tip control.

2.2.2.4.Flexibility and bending

It is an ability to bend with direct pressure (12).This is the ability of a wire to flex on its longitudinal axis while maintaining torque and trackability. This is important when reaching a tortuous lesion. The core of wires are either made of very flexible nitinol or stiff stainless steel, which dictates a guidewire's flexibility. Spring coil tip guidewires have a better bending capacity, whereas, single core guidewire resists it.

2.2.2.5.Support

It is ability to maintain the original shape, wip resistance and carrying capacity of the over the wire device (13). Short tapered tips with high tensile stainless steel core provide superior support.This is the level of support a wire provides. Floppy/light wires were originally designed for balloon angioplasty and provide improved trackability and flexibility. Moderate support wires are used for stenting, offering the needed support to deliver and deploy a stent. Extra support wires are often used for stenting or to support buddy wires.

2.2.2.6.Malleability

It refers to the ability of the coronary guidewire to be shaped or bent without breaking. Nitinol materials are more resistant to breaking, however, they tend to return their original shape in a shorter time which may affect the procedures in a negative way. Stainless steel core with non-polymeric tip is more suitable to manual shaping, however this action may interfere the track and torque ability. For this reason, preshaped guidewires was manufactured to response the operators demands (15,19).

2.2.2.7.Penetrability

It is ability to puncture a lesion. This property is very important in CTO intervention since proximal cap of the CTO lesion is usually tough, and penertability of the guidewires play a major role in crossing the lesion (20). This ability depend on tip composition, tip load, wire support. Penetrability is important feature in the choice and preference of the guidewires.

2.2.2.8.Crossability

It is ability of guidewire to cross lesion with little or no resistance (13). Crossability of the guidewire is important for initial choice and rational guidewire usage.Stiffer wires can usually cross significant lesions more easily.

2.2.2.9.Pushability

It is an amount of the force needed to advance the wire or the ease of advancing the wire once it has penetrated the lesion. This feature usually determined by the lateral support of the wire.

2.2.2.10.Prolapse tendency

Tis tendency of the body of the wirenot to follows the tips around bends. Abrupt and short tapered tips tend to prolapse more frequently. New technologic composite core guidewire usualy show less prolapse tendency.

2.2.2.11.Resiliency

It refers to original tip shape retention. Shaping ribbon tips allow stronger shape retention. Polymeric jacket and nitinol core guidewires also tend to keep their original shape.

2.2.2.12.Radiopacity/visibility

It is ability to visualize guidewire under fluoroscopy. The tips, core and shaft region usually have a different angiographic image. Visibility of the tip is crucial for penetration to CTO segment. Radiopacity also allow to differentiate polymeric portion of the guidewires.

2.2.2.13.Tactile feedback

It is a tactile sensation on a proximal part of guidewires that operatorshas that tells him what the distal end of guidewire is doing. It is a reflection of the tip sensation (13). Non-covered guidewires has a beter tactile sensetion.

2.2.2.14.Lubricity

It is ease of passage through vessel or lesion (12). Non-coated conventional guidewires usually offers more resistance during advancing the guidewires. Polymer coated and hydrophilic guidewires offers less resistance.

In 1977, Andreas Gruntzig performed first coronary angioplasty procedure. He attached a short guidewire directly to balloon catheter tips rather than monorail guidewire system. In 1982, Simpson had described first over the wire balloon system. He used simple movable flexible-tipped guidewires within the balloon catheter (4). Meanwhile, biotechnologic innovations lead to delivery of high performance guidewires which increases the success rate of coronary interventions prominently (Table 1). We going to briefly summarized the features of 0.014 inch coronary guidewires used for cto interventions.

Table 1. Milestones in the CTO guidewire technology.

Year	Innovations	Product
1995	Polymeric coating	Choice PT (Scimed)
1996	Hydrophilic coating	Crosswire (Terumo)
1997	Incremental tip load (drilling concept)	Miracle brand (Asahi)
1998	Tapered tip design	HT Cross-it XT (Guidant)
1998	Combination of tapering with hydrophilic coating and high tip stiffness (≥9 gr) (penetration concept)	Confianza pro (Asahi)
2008	Combination of tapering with polymer and hydrophilic coating in low tip stiffness (<1 gr)	Fielder XT (Asahi)
2010/2011	Composite core tip in low tip stiffness	Sion, Fielder XT-A/XT-R (Asahi)
2013	Combination of composite core tapering polymeric and hydrophilic coating in intermediate stiffness (>1.5 gr, >5 gr) (Deflection and rotation concept)	Gaia brand (Asahi)

This table retrived from the Sianos et al. BMC Cardiovascular Disorders (2016) 16:33

2.2.3.Major CTO Guidewires

Although there are numerous coronary guidewires introduced for use, majority of the operators preferring the guidewires belong to Asahi Intecc, Boston Scientific and Abbot Vascular company. Recently, Terumo and Medtronic also introduced new dedicated coronary guidewires for CTO procedure. We are going to summarize the major guidewires used in CTO procedures.

2.2.3.1.Guidewires for standard procedures

Guidewires composition is usually composed of stainless steel core material with spring coil tip and hydrophilic coatings. Polymer jacket options also available for more slippery property. These guidewires used for usual procedures. In CTO procedure they used for the placement of microcatheter and final stent deployment. So, they just preferred as a supporting biomaterials rather than crossing of the lesion. It means, they are important for the beginning and finalizing of the cto procedure, but they are not essential biomaterials for successfull CTO lesion penetration. Herein, we brieflly summarized the most commonly used coronary guidewires for standard procedure.

Choice Floppy (Boston Scientific, MA, USA)

It is composed of unibody stainless steel core material and spring coil tip material. There is a hydrophilic coating except distal 3 cm tip segment. It has a soft floppy tips and light rail support which gives superior tactile feedback and good steerability.It is usually preferred for frontline lesion. Tip load is 0.5 gram (16).

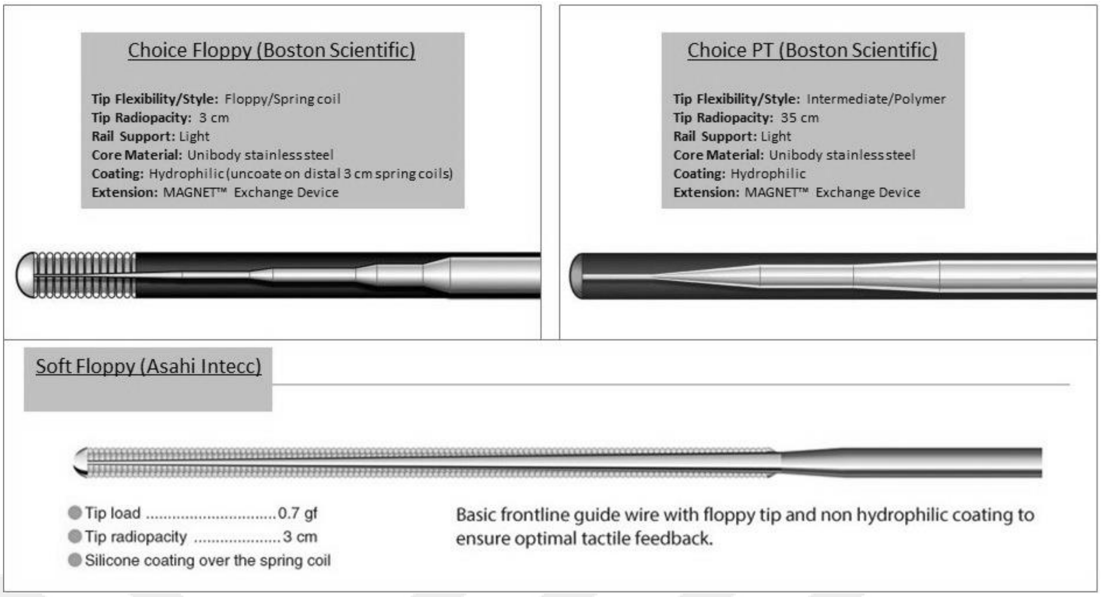
Soft (Asahi Intecc, Nagoya, Japan)

Similar to Choice Floppy guidewire, it has a stainless steel core body and spring coil tip. There is a silicone cover over the spring tip and tip load is 0.7 gram. Contrary to Choice Floppy, Soft guidewire has a hydrophobic coating which bring an optimal tactile feedback. It is usually preferred for frontline lesions (15).

Choice PT(Boston Scientific, MA, USA)

It is composed of unibody stainless steel core material with a hydophilic polymer coated intermediate tip. It is usually preferred for tortouos anatomy (16).

The operators should be carefull about the composition of the guidewires even in the same brand (16). Although PT Floppy and PT2 guidewires classified in a same brand, they has a definitevely different composition (Figure 6). PT Floppy have a stainless steel core with soft tip, whereas PT2 guidewire have a elastic nitinol core and it have a resilient tip which tend to return it’s original straight tip after manual tip shaping.



This image is taken from the official site of Boston Scientific and Asahi Intecc for the demostration of the product.

Figure 5. Basic floppy guidewires composition

1.2.3.2.Guidewires for CTO procedures

Guidewires for standard procedures commonly preferred in cto interventions. However, success rate of procedures with standard instruments is not higher (21). Complication rate and long-term prognosis was also not so good. Dedicated guidewires for CTO procedure increased the procedural success rate recently. Each has special composition and behavioral characterstic and their preference depend on lesion type and initial strategy.

Special features of CTO wires

Penetration force for puncture the proximal fibrous cap, pushability for crossing the CTO segment, steerability for easy manipulation in a varios direction, shaping memory of the tip are the major properties of CTO dedicated guidewires (9).

CTO crossing techniques

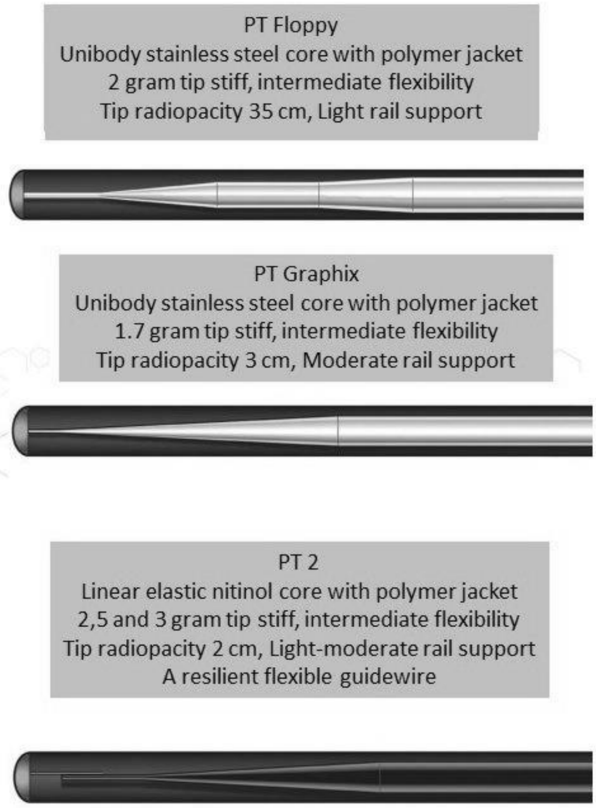
Single wire cross with sliding motion is most commonly preferred tehniques and hydrophilic wires more commonly used in this strategy (22).

Paralel wire with escalation of the guidewire is a provosionel stategy when initial guidewires fail to advance in the lumen. In this strategy, combination of two or more guidewire usually used to cross the lesion.

Step and step down with drilling motion is become more popular after releasing of new biotechnologic guidewires (22). In this technique, there is alternating usage of guidewires with different characteristics. Subsequent use of stiff hydrophobic non-tapered guidewires and polymeric moderate stiff guidewires may ease the crossing of the lesion.

Penetration of tough proximal stump with super stiff, tapered wires usually preferred in tight calcific lesions (23).

In the following section, we will briefly summarized the leading CTO guidewires. Each company has a guidewire series with similar composition for CTO lesion. We are going to focused on the guidewires more commonly preferred and also available in Turkey.

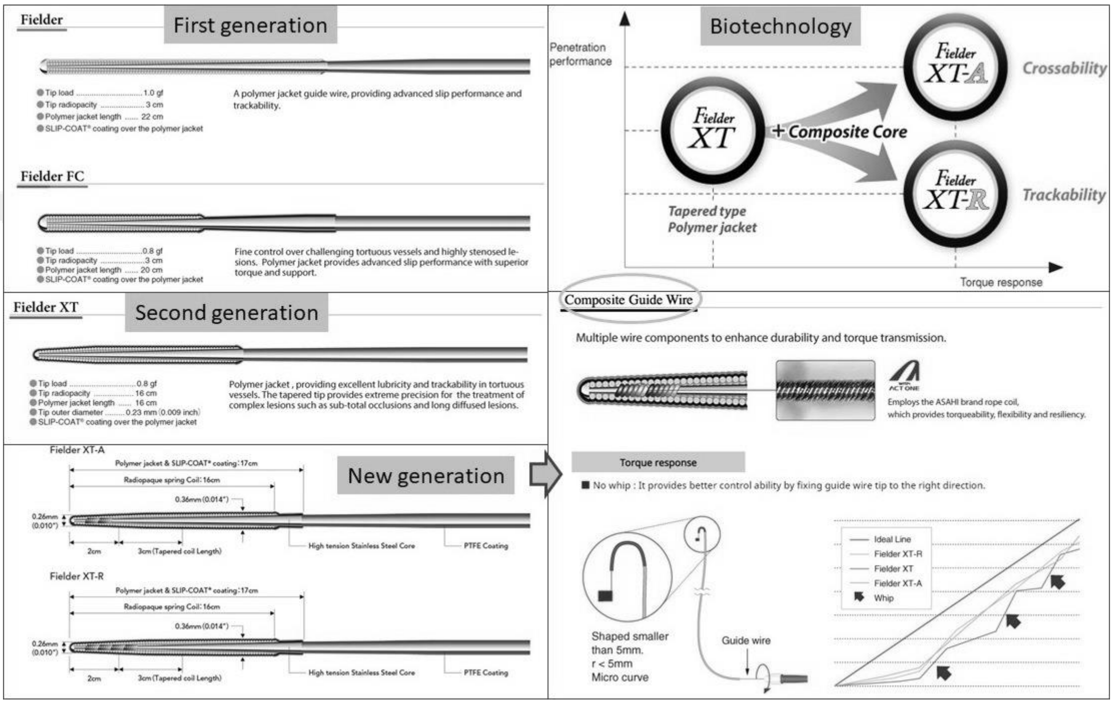


This image is taken from the official site of Boston Scientific for the demostration of the product.

Figure 6. Composition of the PT brand guidewires.

Fielder brand (Asahi Intecc)

It is a fronline guidewires for cto with microchannel. It also preffered in a various state of cto intervention. Basic Fielder series is a polymer jacket guidewires with 1 gram tip load which gives flexibility (9,15,24). There is a specal slip-coat hydrophilic coating over the polymer jacket which enhance the trackability. Biotechnological innovations change the basic composition of the Fielder series over the time (Figure 7). Fielder FC series has a softer tip load with different tapering shape which enhance the torquability and support of the guidewire. Fielder XT series has shorter polymer jacket length with delicated tapered soft tip which enhance the crossability of the guidewire. The outer tip diameter of the Fielder XT is just 0.009 inch. Fielder XT-A and Fielder XT-R the latest generation of Fielder brand. They both has composite core composed of multiple wire rope coil components which enhance durability and torquability. They are superior to previously delivered Fielder series in term of torqueability, flexibility and resiliency. They have wip resistance more duraple tip composition. Fielder XT-R was developed for retrograde cases which has a soft tip. It's superior trackability enables the successfull collateral passage. Fielder XT-A series has a more stiffer tip which support the antegrade crossability (15). Whisper brand of Abbot Vascular is a compatriot of Fielder brand (17).

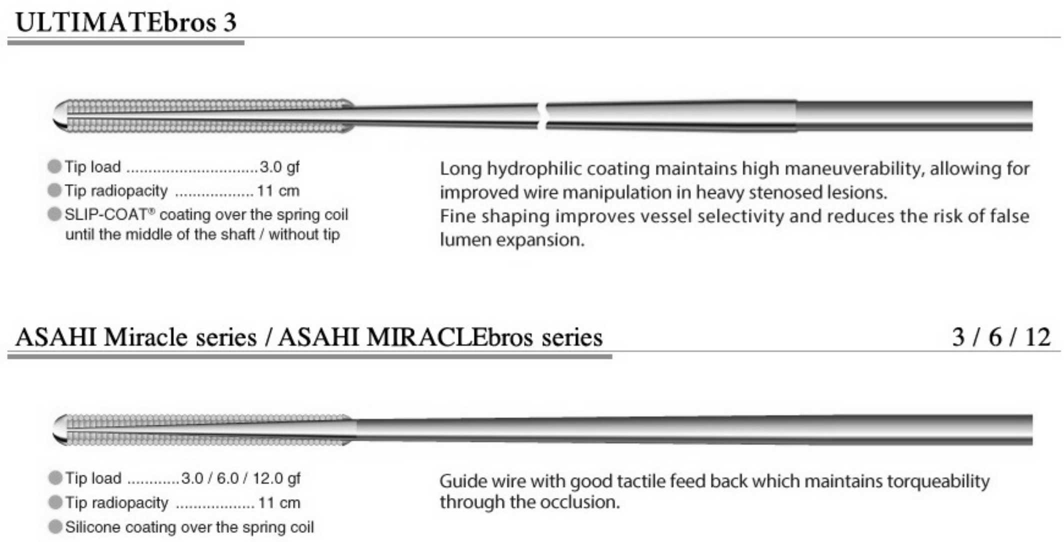


This image is taken from the official site of Asahi Intecc for the demostration of the product.

Figure 7. Biotechnologic development in Fielder guidewires.

Miracle brand (Asahi Intecc)

It as stainless stell core material tapered at the tip which covered with spring coil and silicone (Figure 8). It has a moderate to stiff tip load which is usually preferred in more complex cases (9,15,24). It has superior tactile feedback and good torque transmission. Stiffer tips (3,6,12 gram) enable more strong penetration power (15). It is used in clinical practice more than 20 years. It has a non-tapered tip which limits the penetration power. After the generation of Gaia series, the popularity of the Miracles series was go down. However, it is still commonly preferred in CTO cases due to affordability and relatively cheaper cost. Cross-it brand of Abbot Vascular has a similar features with Miracle brand (17).



This image is taken from the official site of Asahi Intecc for the demostration of the product.

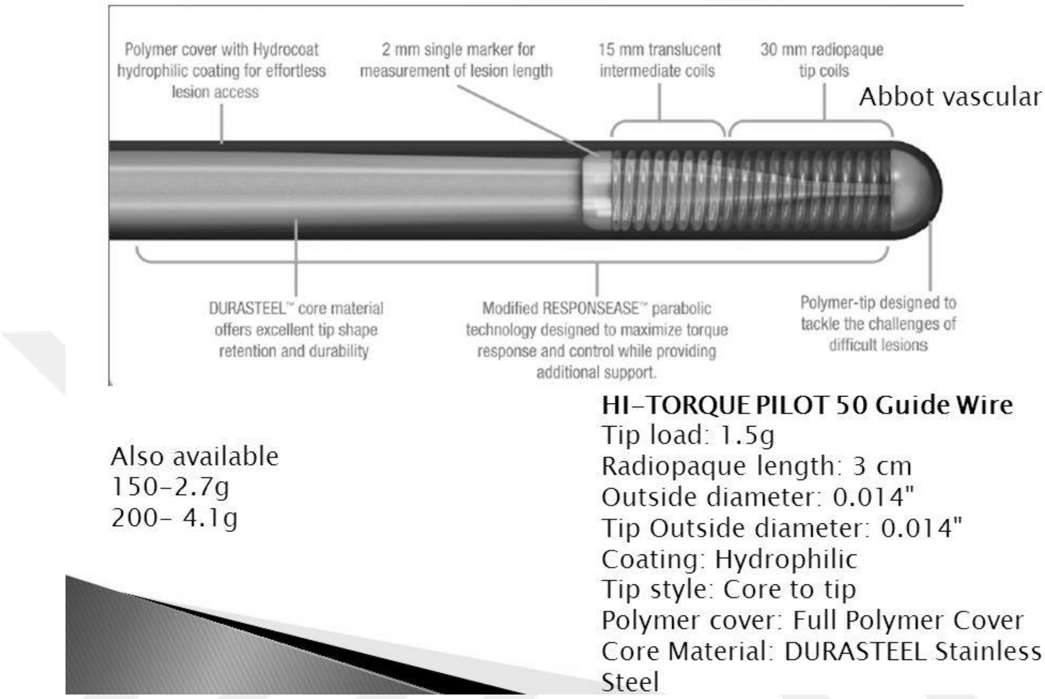
Figure 8. Composition of Ultimatebros and Miracle guidewires.

Ultimatebros brand (Asahi Intecc)

It composition is resemble to Miracle 3 series. Additionaly, it has slip-coat hydrophilic sleeves over the spring coil until the middle of the shaft (9,15,24). The tip is free from the hydrophilic coating (Figure 8). Long hydrophilic coating improves trackability and guidewire movement through the lesion. Fine tip composition reduces the sub-intimal movement and false lumen expansion.

Pilot brand (Abbot Vascular, CA, USA)

It composed of durasteel core material with core to tip design and polymer jacket. It has 3 different tip load (1.5,2.7 and 4.1 gram) which described as Pilot 50-150-200 series (Figure 9). Parabolic core grind provide superior steerability especially in the complex lesion without microchannels (9,17). In clinical practice Pilot 200 is more commonly preferred due it's higher penetraton capacity.

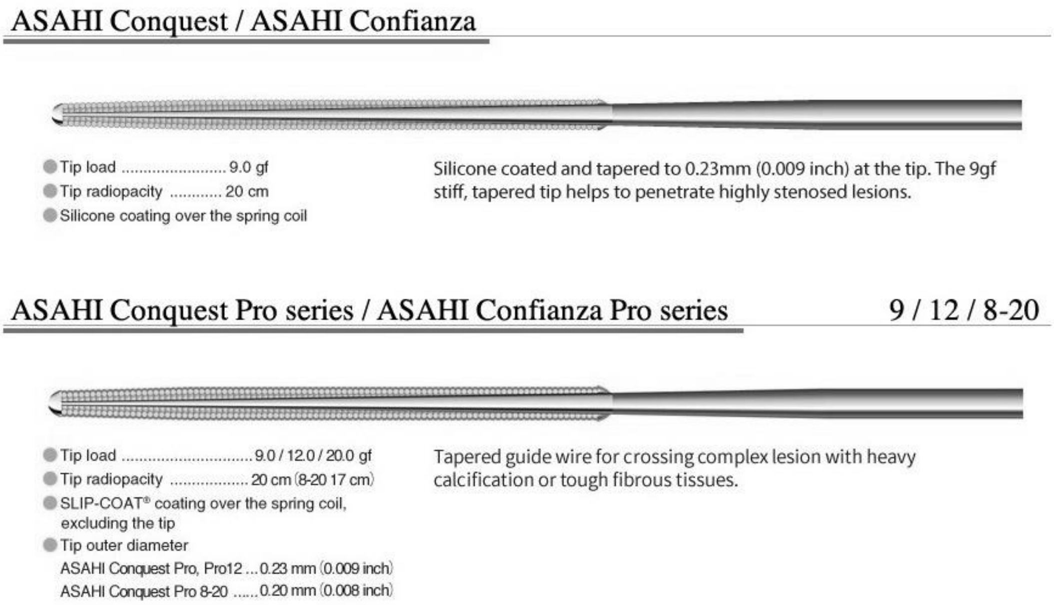


This image is taken from the official site of Abbot Vascular for the demostration of the product.

Figure 9. Composition of hi-torque Pilot guidewires.

Confianza brand (Asahi Intecc)

It has a 9 gram stiff tapered tip with stainless steel core material. Silicone coating over the spring coil help the penetration of the guidewire in highly calcified lesion (Figure 10). The Confianza/Conquest Pro series have a more stiffer tips (9,12,20 gram) and similar to Ultimate series, hydrophilic slip-coat cover the spring coil excluding the tip (9,15). This series usually preffered for the penetration of the tough proximal stump. Progress brand of Abbot Vascular has a simlar features with Confianza brand.



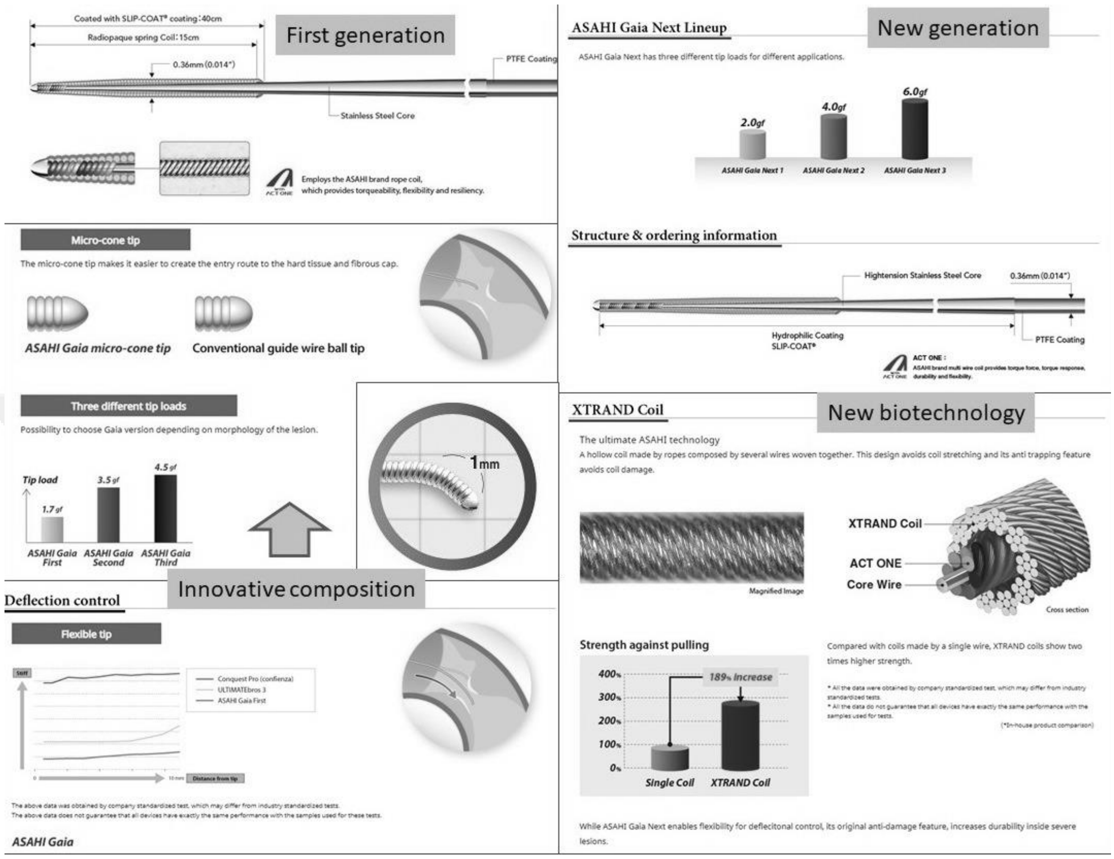
This image is taken from the official site of Asahi Intecc for the demostration of the product.

Figure 10. Composition of Confianza guidewire brand.

Gaia brand (Asahi Intecc)

It has a different composition comparing to conventional guidewires which open a new era in CTO interventions (11,20,22). It has a stainless steel tapered core material with high technology composite core tip composition. Tip structure enable higher performance similar to stiffer tipp guidewires (9,15). However, it has a beter tip movement and deflection motion which is not prominent in conventional stiffer tip guidewires.

Pre-shaped tip structure give a superior stability to tip composition which may be impaired by the manual tip shaping. It has 3 different tip load with hydrophilic slip-coat covering. Micro-cone shaped tip composition provides powerfull penetration. It has a superior trackability, torque control, resiliency and crosability comparing to older conventional brands. Recentl delivered GaiaNext series has additional features (Figure 11). Xtrand coil tip technology decrase the risk of trapping of the guidewire and also increases the torque control. GaiaNext series has a higher tip loads comparing to initial series and GaiaNext series will replace the older series in the near future. Afordability and expensive price is the major limitation for the GaiaNext series currently.

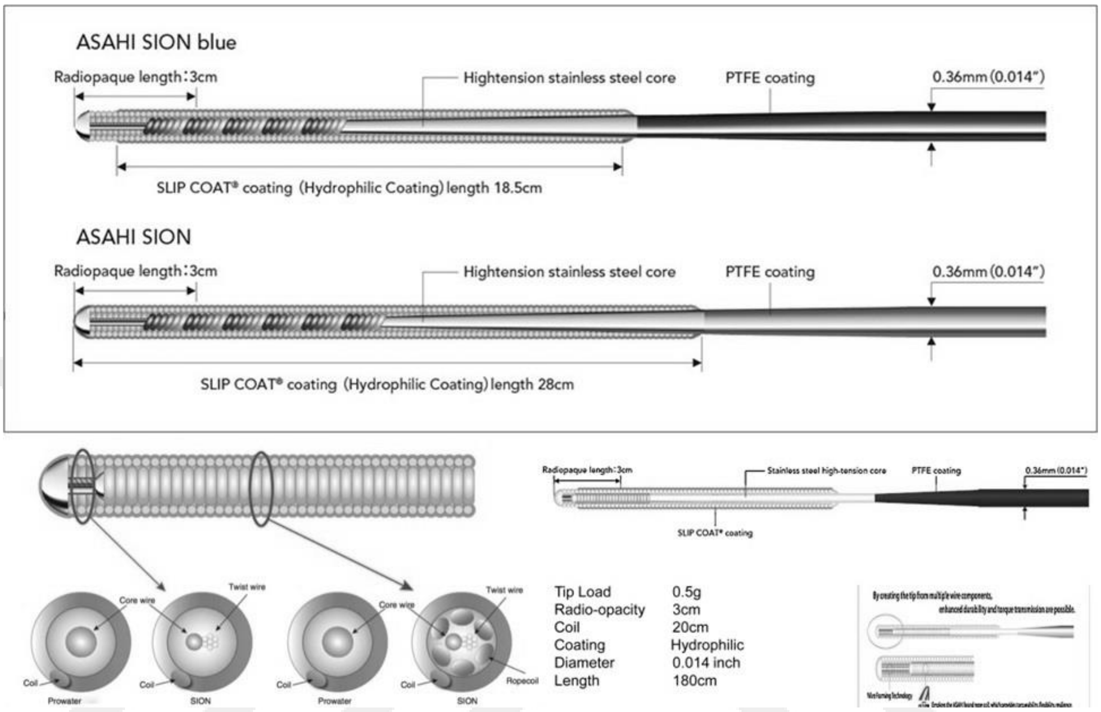


This image is taken from the official site of Asahi Intecc for the demostration of the product.

Figure 11. New generation Gaia guidewires.

Sion brand (Asahi Intecc)

It is first line choice for retrograde strategy and collateral crossing (9,25). It has a delicated tip composition. It has a composite core technology, tapered core material acompany to twisted wire which was surrounded by the rope coil and spring wires The tip structure is resistant to kink and knuckle formation comparing to conventional guidewires (15). All the wire is coated with hydropilic material to enhance crossability. Sion blue series has a different tip composition with15 mm silicone coating instead of full hydrophilic coat (Figure 12). Sion blue series has a excellent support in device deployment. Recently released Sion black series has an additional polymer jacket which provide beter lubricity. Tip load of Sion black is 0.8 gram and it has a superior flexibility comparing to basic Fielder series.

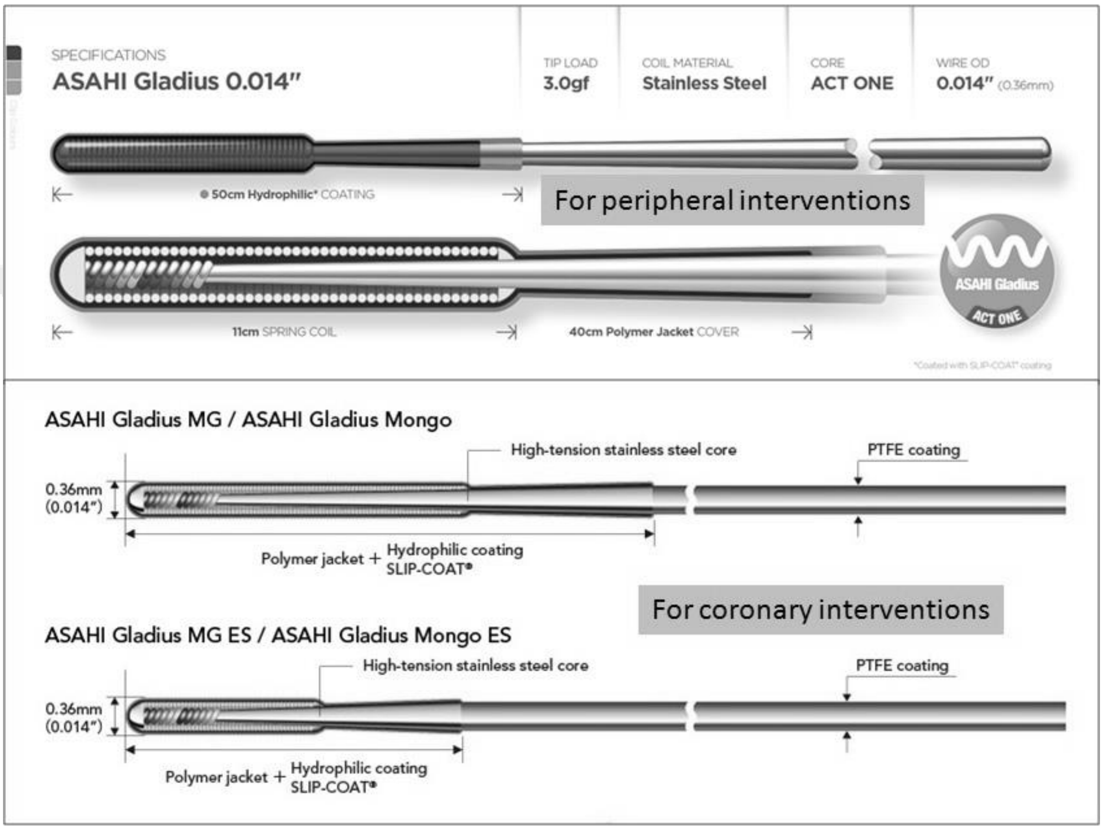


This image is taken from the official site of Asahi Intecc for the demostration of the product.

Figure 12. Composition of Sion and Sion Blue series guidewires.

Gladius brand(Asahi Intecc)

It is a polymer jacket guidewire with 3 gram tip load. It has a high tensile stainless steel core material covered by PTFE. It is actually designed for peripheral interventions particularly below-the-knee lesions (19,15). It manufactured with composite core technology which provide acceptable torque control, support and penetration performance in a same guidewire (Figure 13). It has a durable tip compositon that retain it’s original shape which is preshaped 1 mm. Although it is released for peripheral interventions, it began to preferred in cto procedures by the many operators as a off-label usage. It is also 0.014 inch diameter which is suitable for coronary interventions also. Meanwhile, the manufacturer recognised this situation and they released a coronary version of Gladius series as Gladius MG. Both peripheral and coronary Gladius belong ro same composite core technology, but coronary version belong to shorter spring coil (11 cm versus 8 cm). ES series has longer core with shorter spring coil(3 cm) to provide maximal support. Most of the catheter laboratory just hold peripheral series rather than coronary series.



This image is taken from the official site ofAsahi Intecc for the demostration of the product.

Figure 13. Peripheral and coronary Gladius guidewire composition

3.MATERIALS AND METHODS

3.1.Patients selection

This investigation was performed in the catheter laboratovary of Acibadem Hospitals. The investigation is a cross-sectional, retrospective - prospective and observational analysis of the subsequent coronary chronic total occlusion procedures. The name and the individual data of the patients did not revealed in the investigation. Between 1 January 2019 and 30 April 2020, a total of 177 patients with indication of coronary CTO procedure were included in this study. Since, our primary end-point is evaluation of biomaterials used in the procedure, the cases with incomplete recordings and lacking of clinical and laboratory data were excluded from the study.

3.2.Protocol and Procedure

Upon admission, patients were evaluated with anamnesis and physical examination. Then, blood samples were taken for laboratory analysis. Echocardiography was performed before the procedure and hypokinesia in the CTO lesion territory was assessed in detail. The CTO procedure recording of the patients were checked with the permission of the catheter laboratory directors. Images of each procedure was evaluated once more and J-CTO score and Eurocto score of the each lesion was calculated according to previously defined criteria (Figure 14, Table 2). All the biomaterials including catheters, guidewires, balloon and stent materials were analysed extensively. The techniques preferred in the procedure was also recorded. The 0.014 inch guidewire usage evaluated according to clinical and lesional characteristic, techniques, J-CTO and Eurocto scores. Number of guidewires, initial choice and final guidewire that crossed the lesion was noted. Determinants of crossability of initial choice guidewire was evaluated with further statistical analysis. Since CTO interventions are complex and time-consuming procedure; the contrast amount, procedural time, fluoroscopy duration was also recorded for each procedure.

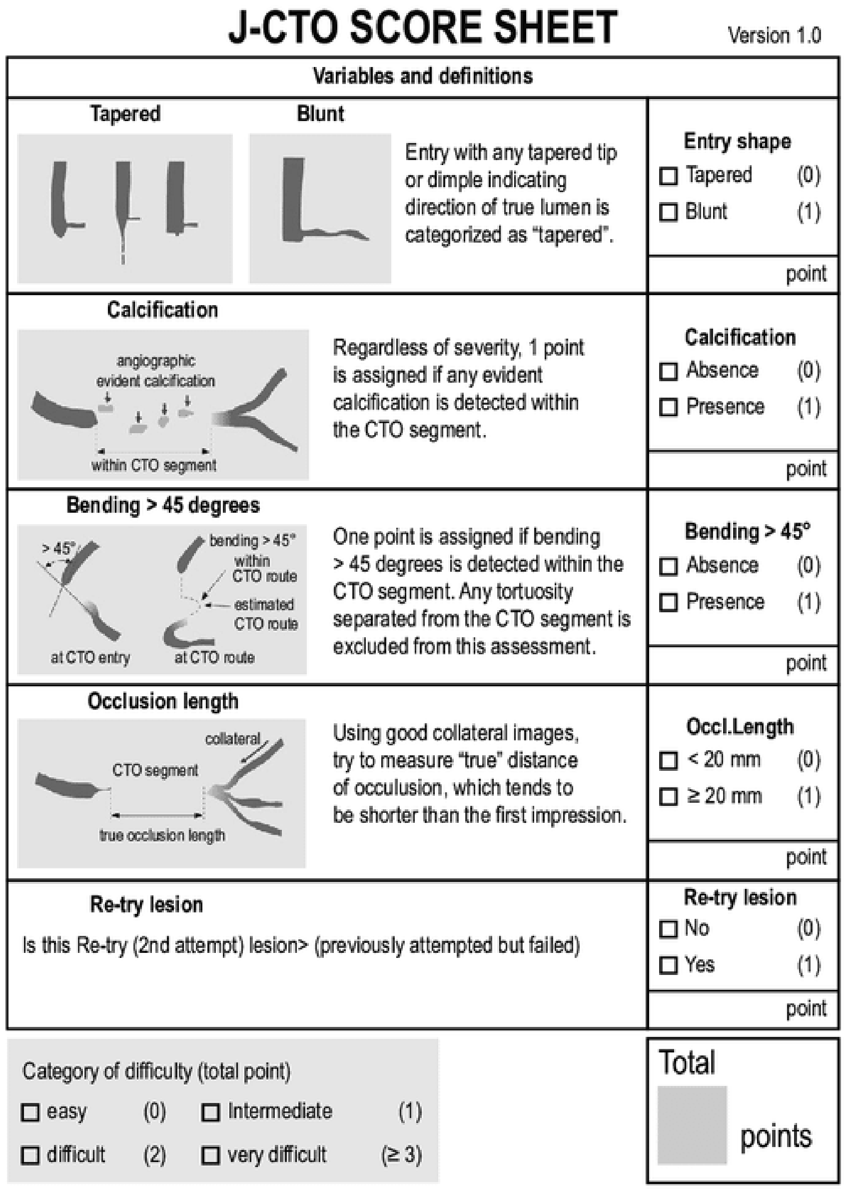
After the procedure, all the patients were followed in the intensive care unit for a day. Serum creatinine concentrations were measured before discharge.

3.3.Definition

Chronic total occlusion was defined as total occlusion of one major epicardial coronary vessel at least 3 months duration or indetermined time. The complexity of the CTO lesion and difficulty of the procedure were analysed according to J-CTO and Eurocto scores. J-CTO 0 score was accepted as a easy case, J-CTO 1 defined as intermediate case, J-CTO 2 was defined as difficult case and J-CTO≥3 was accepted as very difficult cases. Body mass index was calculated as a weight (kg)/ height^2 (m) and BMI≥30 was defined as a obesity. Hypertension (HT) was defined as previoususe of anti-hypertensive medications or a systolic pressure >140 mmHg or a diastolic pressure >90 mmHg on at least two separate measurements. Diabetes mellitus (DM) was defined according to the patients' history, use of insulin or anti-diabetic agents, fasting glucose >126 mg/dL, or random blood glucose level >200 mg/dL. Dyslipidemia was defined as either low density lipoprotein (LDL) cholesterol >100 mg/dL or triglycerides >150 mg/dL, or both, or drug use for dyslipidemia. Smoking was defined as current regular use of cigarettes or cigars within the last six months. Renal function was assessed by the estimated (eGFR GFR) using the formula of Modification of Diet in Renal Disease Study (MDRD).

The MDRD formula is (186 × serum creatinine – 1.154 × age – 0.203) [× 0.742 if female] × [1.212 if black].

Guidewires was classified according to their coatings and tip stiffness. Tip weight load <1 gram accepted as soft guidewire and tip weight load≥9 gram was defined as stiff guidewire. According to tip coatings, the guidewire was classified as polymeric and non-polymeric guidewires. The number of 0.014 inch guidewires also classified as optimal (1-3), acceptable (4-6), overuse (7-9) and overmuch (≥10).



This image is taken from the Japenese Multicenter CTO registry for the demostration of the J-CTO chart

Figure 14. Chart for J-CTO score calculation

Table 2. Chart for Eurocto score (CASTLE score) calculation

Variable	Points
CABG (Previous)	1
Age (>70)	1
Stump (Blunt or none)	1
Tortuosity (severe or unseen)	1
Length (>20 mm)	1
Extent of calcification	1
Total points	6

CABG:Coronary artery bypass grafting

3.4.Statistical analysis

Statistical analyses were performed using SPSS 21.0 software (SPSS Inc., Chicago, IL, USA). Mean ± standard deviation, median and maximum–minimum were used for continuous variables, while percentages were used for categorical variables. The student t-test and one way Anova test was used for evaluating continuous variables between groups. Categorical variables were compared using the chi-square test and Fisher’s exact test. Further analysis performed according to initial and final choice 0.014 inch guidewires. Preference of the guidewires was analysed according to procedural technique and J-CTO and Eurocto scores. Pearson and Spearman correlation analysis was performed to define the determinants of crossability of first choice guidewire. Finally, univariate and multivariate regression analyses were performed to analyse the independent predictors of crossability of initial choice guidewire. The baseline variables for which evident significance ($p < 0.10$) was found by univariate analysis were included in the multivariate logistic regression analysis. The results of the model were reported as a 95% confidence interval (CI) and p-values. All p-values were two-sided in the tests and p-values less than 0.05 were considered to be statistically significant.

3.5.Ethical concern

This study was approved by the Ethics Committee of the Acibadem Mehmet Ali Aydinlar University (Date:19.12.2019; decision number:2019-20/22) (Appendix 1).

4.RESULTS

4.1.Demographic and clinical features

Totally 177 CTO procedure was performed and success rate was 91.4 %. The lesion could not be crossed in the 17 cases which recorded as failed procedure. The baseline demographic and clinical characteristics of the patients are summarized in Table 3. The mean age was 62.4 ± 10.5, ranging from 29 to 86 years, and 141 patients (79.7%) were male. The prevalence of HT and DM were 54.2% and 37.3%, respectively. The incidence of the HT was parallel to Turkish population, whereas, the proportion of diabetic patients was quietly high. The smoking status was higher parallel to male predominance. Current smoker rate was 32.2% and ex-smoker rate was 20.3%. The mean BMI of sample was 28.27±4.42 which described as overweight. Nearly 30% of the cases have a anamnesis of previous MI. Previous CABG history was 18.1%. Aproximately ¾ of the patients presented with stable angina pectoris and half of the patients showed segmental left ventricular wall hypokinesia on echocardiographic evaluation. The renal function of the patients was mostly normal with an average 90.3±31.8 ml/min GFR value. Pre-procedural and post-procedural creatinine level was similar (1.00±0.33 vs 1.04±0.34).

Table 3. Baseline demographic characteristics, clinical features, laboratory results of the patients.

Variables	% (n: 177)	Variables	% (n: 177)
Age (years)	62.4 ± 10.5	Stable angina pectoris	75.7 % (134)
Range;	29-86 years	CCS Class 1	4.5 % (8)
Sex		CCS Class 2	31.6 % (56)
Male	79.7 % (141)	CCS Class 3	35.6 % (63)
Female	20.3 % (36)	CCS Class 4	4 % (7)
Presence of Diabetes mellitus	37.3 % (57)	Unstable angina	4.5 % (8)
Presence of Hypertension	54.2 % (96)	Previous MI	29.3% (52)
Presence of dyslipidemia	43.5% (77)	Previous CABG	18.1% (32)
Smoking		Documentation of ischemia	29.9% (53)
Current smoker	32.2% (57)	LV EF	
Ex smoker	20.3% (36)	>50%	66.7% (118)
BMI (kg/m^2)	28.27±4.42	35-50%	28.8% (51)
Initial creatinine (mg/dl)	1.00±0.33	<35%	4.5% (8)
Post-procedural creatinine (mg/dl)	1.04±0.34	Hypokinesia in cto territory	50.3% (89)
Initial GFR (ml/minutes)	90.3±31.8	Akinesia in cto territory	2.3% (4)

BMI: Body mass index, GFR: Glomerular filtration rate,CCS: Canadian Cardiovascular Society, MI: Myocardial infarction, CABG: Coronary artery bypass grafting, LV EF: Left ventricular ejection fraction

4.2.Angiographic and procedural features

Angiographic features of the CTO lesion was summarized in Table 4. Right coronary artery was the most common vessel having CTO segment (47.5%).Middle and proximal segmental location was more common comparing to distal and ostial location. The lesion characteristics which aggravate the difficulty of the procedure was below the 50% (In-stent stenosis -13%, multilevel occlusion - 11.9% and bifurcation on the cto segment-33.9%) J-CTO and Eurocto scores revealed that totally 55% of the lesion was either easy or intermediate difficulty and number of the very difficult cases was definitevely low (18.2% of the cases). Radial access was preferred in the 58.8% of the cases and conlateral injection was performed in the half cases. In concordance with higher number of J-CTO score 0-1 grups, single wire crossing was come to the forefront as major procedural technique which followed by step up – step down strategy (60.5% and 23.2 % respectively).

Table 4. Angiographic, technical and procedural features of chronic total occlusion lesions.

Variables	% (n: 177)	Variables		% (n: 177)
Vessel		J-CTO Score		1.42±1.16
LAD	32.8 % (58)		0	26.0 % (46)
LCX	19.8 % (35)		1	28.2 % (50)
RCA	47.5 % (84)		2	27.7 % (49)
Segment			3	13.6 % (24)
Ostial	6.8 % (12)		4	4.0 % (7)
Proximal	36.7 % (65)		5	0.6% (1)
Mid	46.3% (82)	EuroScore		1.44±1.18
Distal	10.2 % (18)		0	23.2 % (41)
In-stent occlusion	13% (23)		1	31.1 % (55)
Multilevel occlusion	11.9% (21)		2	32.8 % (58)
Bifurcation in cto segment	33.9 % (60)		3	6.8 % (12)
Radial access	58.8 % (104)		4	4.0 % (7)
Contra-lateral injection	53.1 % (94)		5	1.7% (3)
Retrograde approach	4 % (7)		6	0.6% (1)
Guiding catheter		Procedural technique		
6F	16.9 % (30)		Single wire cross	60.5 % (107)
7F	83.1 % (147)		Parallel wire cross	6.2 % (11)
Successfull procedure	90.4% (170)		Step up – step down	23.2 % (41)
			Dissection and re-entry	8.5 % (15)
			Reversed cart	1.7 % (3)

LAD: Left anterior descending artery, LCX: Left circumflex artery, RCA: Right coronary artery, F: French, J-CTO: Japan registry of chronic total occlusion

4.3.Guidewire choice and preference

Guidewire choice and their characteristics was summarized in Table 5. The average use of guidewire number was 4.32±2.39 and in the 47.5% of the cases, 1-3 guidewire used during procedure which could be commented as economical and optimal use of guidewires Initial guidewire choice for procedure was usually polymeric guidewires and Fielder and Pilot brand was most commonly preferred guidewires as a first choice (26.6% and 36.2%). Moderate and soft tip load guidewires was preferred rather than stiff tip guidewires as a first choice (Moderate tip load-55.4%, stiff tip load-12.4%). Stiffer tip and non-polymeric guidewires was more frequently preferred as a final guidewire comparing to initial choice. Pilot, Fielder and Gaia brands was most successfull guidewires in term of crossing the CTO segment.

Table 5. Type and structural features of 0.014 inch coronary guidewires used for chronic total occlusion procedure.

Variables	% (n: 177)	Variables	% (n: 177)
Guidewire number	4.32±2.39	Final guidewire	
1-3	47.5 % (84)	Fielder brand	22.6 % (40)
4-6	36.7 % (65)	Miracle brand	5.1 % (9)
7-10	12.4 % (22)	Pilot brand	26.6 % (47)
>10	3.4 % (6)	Gaia brand	13 % (23)
Initial guide wire		Confianza brand	9 % (16)
Fielder brand	26.6 % (47)	Ultimate brand	1.7% (3)
Miracle brand	6.2% (11)	Sion brand	2.3 % (4)
Pilot brand	36.2 % (64)	PT brand	1.7 % (3)
Gaia brand	2.3% (4)	Gladius brand	5.6 % (10)
Confianza brand	11.3% (20)	Progress brand	2.3 % (4)
Ultimate brand	6.8 % (12)	Cross-it brand	0,6 % (1)
Sion brand	5.6 % (10)	Failed procedure	9.6 % (17)
PT brand	2.3 % (4)	Final guidewire type	
Gladius brand	2.3 % (4)	Polymeric	56.5% (100)
Progress brand	0.5 % (1)	Non-poylmeric	33.9 % (60)
Initial guidewire type	16.9 % (30)	Final guidewire stiffness	
Polymeric	67.2 % (119)	Soft (<1 gram)	24.9 % (44)
Non-poylmeric	32.8 % (58)	Moderate (1-9 gram)	47.5 % (84)
Initial guidewire stiffness		Stiff (≥ 9 gram)	18.1 % (32)
Soft (<1 gram)	32.2 % (57)	Same initial – final guidewire	44.1% (78)
Moderate (1-9 gram)	55.4 % (98)		
Stiff (≥ 9 gram)	12.4 % (22)		

Although the Gaia brand was not favorite for initial choice guidewires, it was final choice in the 13% of the cases. The guidewires special for CTO procedure was preferred in the majority of the cases. PT brand which accepted as a standard guidewire for simple procedure used only 2.3% of the cases as a initial guidewire.

4.4.Crossability of initial guidewires

Crossability of the initial guidewires is important for optimal guidewire usage. In such scenario, first choice and final crossing wire should be the same. We observed that logical preperation for the CTO procedure and reasonable guidewire choice would lead to lesser guidewire usage. Initially preferred guidewire was also crossing final wire in 78 patients (44.1%). Lesion characteristic and techniques have a major influence in the crossability of the guidewires. As it was accepted, single wire crossing technique was the initial strategy in the same initial-final guidewire group (88.5%). An avarage guidewire number was definetevely low comparing to opposing group (Table 6). As the complexity of the lesion was increased, the crossability of the initial guidewire was dropped. J-CTO 0-1 groups have a highest probability of same guidewire as a initial and final choice. Lesion location did not affect the crossability of first choice guidewire. Lower number of guidewires and same initial and final guidewire also have some important clinical consequences. In the same initial-final guidewire group, there is a less use of balloon and stent number and total length of stent was also shorter which predict the lower restenosis rate. Not surprisingly, the procedural duration and fluoroscopy time was also shorter which is favorable factor for radiation dose. The amount of conrast use was also lower in this group which associated with lower rate of contrast induced nephropathy (Table 6).

Polymeric and moderate tip stiff guidewires have a superior crossability (Table 6). Pilot 200, Pilot 50 and Fielder XT have higher crosability rate as a first-choice guidewire (30.8%, 20.5% and 20.5%). Even within the same brand, there was a opposing results. Contrary to Fielder XT, crossability of the Fielder FC was not good (1.3% vs 7.1 %). This result may indicate that, distal tip composition is crucial in the crossability. Within the non-polymeric groups, Confianza 9 was relatively higher likelyhood of lesion penetration as a initial choice guidewire.

Crossing of the lesion with initial guidewire also has some important infuences on the procedural result. Floroscopy duration was shorter in the same initial-final guidewire group which decrease the risk for radiation exposure (22.2±13.1 vs 45.6±24.4 minutes, p<0.01). Contrast amount was also lower which decrease the risk of contrast nephropathy (242±114 vs 362±173 ml, p<0.01). Total stent length and stent nummer was also lesser in same initial-final guidewire group which has a important impact on long-term stent patency (50.6±21.8 vs 65.7±33.0 mm, p:0.01). Use of lesser balloon catheter also decrease the total cost of the procedure in the same initial-final guidewire group.

4.5.Procedural strategy and guidewire choice

Table 8 reveal the impact of procedural strategy on the guidewire choice. Polymeric Pilot brands is most common initial guidewire choice in the single wire cross technique (41.1%). Polymeric Fielder brands was more commonly preferred for paralel wire technique (45.5%). Non-polymeric Gaia and Confianza brand was preferred in Step up –Step down strategy and dissection and re-entry technique. Soft guidewires are dominant choice for retrograde approach.

4.6.Procedural difficulty and guidewire choice

Lesion characteristics are the most important issue which influence on both strategy and guidewire choice. Several CTO scores was previously described to estimate diffuculty and crossability of the CTO lesion. J-CTO score is the first chart defined for CTO lesion. We performed the correlation analysis between J-CTO score and guidewire preference and performance (Table 9). Polymeric jacket guidewires was preferred in J-CTO 0-1 group more commonly. Whereas, rate of non-polymeric guidewires was relatively more commonly used in J-CTO 3-4. Pilot and Fielder brands was most common preferred polymeric guidewires as a initial choice. Confianza brand was most common preferred non-polymeric guidewire for J-CTO 2-3-4 groups. Avarage number of guidewire usage was also statistically significant in correlation with J-CTO Score. There was a linear correlation between J-CTO score and guidewire number. More complex cases (J-CTO 2-4) was associated with higher number of guidewires ($p<0.001$). Final guidewire type and stiffness did not differ statistically. However, polymeric Pilot brands was prominently more successfull in J-CTO 0-1 group. Non-polymeric Gaia brand has a superior crossability in J-CTO 2-4 group (p:0.04). Crossability of initial choice guidewire has a close relationship with J-CTO score. Same initial-and final guidewire was 71.7% in J-CTO 0 group, which dropped to 14.7% in J-CTO 4 group ($p<0.001$). This analysis showed that crossability of initial guidewires are higher in J-CTO 0-1 group and gradually decline as score increases.

Eurocto score another chart for assessing the procedural success of CTO lesion which described by Eurocto club. Herein, we also performed the correlation analysis between Eurocto score and guidewires performance (Table 10). The results was similar to J-CTO score analysis. Eurocto 0-1 group was signficantly associated with fewer guidewire usage. Avarage guidewire number was below the 4 in Eurocto 0-1 group. On contrary, there was a more than 4 guidewire usage in Eurocto 3-6 group ($p<0.001$). Non-polymeric guidewires was preferred dominantly in Eurocto 0-1 group (80.5 % and 80% (p:0.001). Similar to J-CTO analysis Pilot and Fielder brands was more commonly preferred as initial guidewires in Eurocto 0-1 group (p:0.06). Pilot guidewire has a superior crossability in Eurocto 0-1 group, whereas Gladius brand was more successfull in Euroscore 2-4. The distribution of the rest of the guidewires was similar (p:0.39). Final guidewire type and stiffness did not differ between Eurocto score. Moderate stiff tip guidewires was more commonly preferred as initial guidewire in Eurocto 0-1 group (p:0.01). Crossability of the initial choice guidewire was over the 50% in Eurocto 0-1 group (68.3%, 58.2%, $p<0.001$). However, penetration rate of initial guidewires was quitely lower in Eurocto score 3-6 groups.

Table 6. Clinical and angiographic predictors of first-choice guidewire and it's crossability through the CTO segment.

Variables	Same initial-final guidewire (+)	Same initial-final guidewire (-)	*p*
Age (years)	63.41±10.9	61.74±10.2	0.30
Sex			0.07
Male	71.8 % (56)	84.8 % (84)	
Female	26.9 % (21)	15.2 % (15)	
BMI(mg/dl)	27.9±4.65	28.5±4.23	0.42
Initial creatinine (mg/dl)	0.96±0.30	1.04±0.36	0.12
GFR (ml/minutes)	64.2±22.6	68.7±21.3	0.76
LV EF			0.07
>50%	73.1 % (57)	61.6 % (61)	
35-50%	20.5 % (16)	35.4 % (35)	
<35%	6.4 % (5)	3.0 % (3)	
Hypokinesia in cto territory	41 % (32)	57.6 % (57)	0.09
Procedural technique			<0.01
Single wire cross	88.5 % (69)	38.4 % (38)	
Parallel wire cross	1.3 % (1)	10.1 % (10)	
Step up – step down	5.1 % (4)	37.4 % (37)	
Dissection and re-entry	5.1 % (4)	11.1 % (11)	
Reversed cart	0% (0)	3 % (3)	
Radial access	55.1%(43)	61.6% (61)	0.38
Kontralateral contrast injection	48.7% (38)	56.6% (56)	0.29
J-CTO Score	0.83±0,88	1.89±1.13	<0.01
0	42.3 % (33)	13.1 % (13)	
1	37.2 % (29)	21.2 % (21)	
2	16.7 % (13)	36.4 % (36)	
3	2.6 % (2)	22.2 % (22)	
4	1.3% (1)	6.1 % (6)	
5	0% (0)	1% (1)	
Eurocto score	0.93±0.90	1.84±1.23	<0.01
Target Vessel			0.89
LAD	34.6 % (27)	31.3 % (31)	
LCX	19.2 % (15)	20.2 % (20)	
RCA	46.2 % (36)	48.5 % (48)	
CTO segment			0.50
Ostial	5.1 % (4)	8.1 % (8)	
Proximal	33.3 % (26)	39.4 % (39)	
Mid	52.6 % (41)	41.4 % (41)	
Distal	9 % (7)	11.1 % (11)	
Guidewire number	2.85±1.31	5.48±2.43	<0.01
Ballon number	2.85±1.44	3.20±1.88	0.18
Stent number	1.58±0.70	1.91±0.91	0.01
Stent length (mm)	50.6±21.8	65.7±33.0	0.001
Fluoroscopy duration	22.2±13.1	45.6±24.4	<0.01
Contrast amount (ml)	242±114	362±173	<0.01
Total	44.1 % (78)	55.9 % (99)	

BMI: Body mass index, GFR: Glomerular filtration rate, LV EF: Left ventricular ejection fraction J-CTO: Japan registry of chronic total occlusion, LAD: Left anterior descending artery, LCX:Left circumflex artery, RCA: Right coronary arterY, CTO: Chronic total occlusion,

Table 7. Distributions of guidewire type, number and brands according to crossability of initial choice guidewire.

Variables	**Same initial-final guidewire (+)**	**Same initial-final guidewire (-)**	***p***
Initial guidewire type			<0.001
Polymeric	82.1 % (64)	55.6 % (55)	
Non-polymeric	17.9 % (14)	44.4 % (44)	
Initial guidewire stiffness			0.07
Soft (<1 gram)	28.2 % (22)	35.4 % (35)	
Moderate (1-9 gram)	64.1 % (50)	48.5 % (48)	
Stiff (≥ 9 gram)	7.7 % (6)	16.2 % (16)	
Guidewire number			<0.001
1-3	82.1 % (64)	20.2 % (20)	
4-6	15.4 % (12)	53.5 % (53)	
7-10	2.6 % (2)	20.2 % (20)	
≥10	0% (0)	3.4% (6)	
Guidewire brand			0.005
Fielder FC	1.3 % (1)	7.1 % (7)	
Fielder XT	20.5 % (16)	14.1 % (14)	
Fielder XT-A	1.3 % (1)	3.0 % (3)	
Fielder XT-R	5.1 % (4)	1.0 % (1)	
Miracle 3	1.3 % (1)	1.0 % (1)	
Miracle 6	3.8% (3)	6.1 % (6)	
Miracle 12	0% (0)	0% (0)	
Pilot 50	20.5 % (16)	12.1 % (12)	
Pilot 150	1.3 % (1)	0 % (0)	
Pilot 200	30.8 % (24)	11.1 % (11)	
Gaia 1	0 % (0)	1.0 % (1)	
Gaia 2	1.3% (1)	1.0 % (1)	
Gaia 3	0 % (0)	1.0% (1)	
Confianza 9	7.7 % (6)	14.1 % (14)	
Sion	1.3 % (1)	9.1 % (9)	
Sion black	0 % (0)	0 % (0)	
Ultimate 3	2.6 % (2)	10.1 % (10)	
PT 2	0 % (0)	4.0 % (4)	
Gladius	1.3 % (1)	3.0 % (3)	
Progress 200	0 % (0)	1.0 % (1)	
Total	44.1 % (78)	55.9 % (99)	

P<0.05 is indicated as significant

Table 8. Distribution of first-choice and final crossing guidewires characteristics according to procedural technique.

Variables	Single wire	Parallel wire	Step up Step down	Dissection re-entry	Reversed cart	*p*
Guidewire number	3.63±2.23	4.27±1.19	5.36±2.26	5.80±2.56	7.66±2.08	<0.001
1-3	65.4%(70)	36.4%(4)	19.5%(8)	13.3%(2)	0%(0)	
4-6	24.3%(26)	63.6%(7)	53.7%(22)	60.0%(9)	33.3%(1)	
7-10	7.5%(8)	0%(0)	24.4%(10)	20.0%(3)	33.3%(1)	
>10	2.8%(3)	0%(0)	2.4%(1)	6.7%(1)	33.3%(1)	
Initial guide wire						0.01
Fielder	25.2%(27)	45.5%(5)	24.4%(10)	26.7%(4)	33.3%(1)	
Miracle	5.6%(6)	9.1%(1)	7.3%(3)	6.7%(1)	0%(0)	
Pilot	41.1%(44)	27.3%(3)	31.7%(13)	26.7%(4)	0%(0)	
Gaia	0.9%(1)	0%(0)	2.4%(1)	13.3.%(2)	0%(0)	
Confianza	5.6%(6)	9.1%(1)	22.0%(9)	26.7%(4)	0%(0)	
Ultimate	7.5%(8)	9.1%(1)	7.3%(3)	0%(0)	0%(0)	
Sion	8.4%(9)	0%(0)	0%(0)	0%(0)	33.3%(1)	
PT	2.8%(3)	0%(0)	0%(0)	0%(0)	33.3%(1)	
Gladius	1.9%(2)	0%(0)	4.9%(2)	0%(0)	0%(0)	
Progress	0.9%(1)	0%(0)	0%(0)	0%(0)	0%(0)	
Initial guidewire type						0.57
Polymeric	71.0%(76)	72.7%(8)	61.0%(25)	53.3%(8)	66.7%(2)	
Non-poylmeric	29.0%(731)	27.3%(3)	39.0%(16)	46.7%(7)	33.3%(1)	
Initial wire stiffness						0.01
Soft (<1 g)	35.5%(38)	36.4%(4)	19.5%(8)	26.7%(4)	100%(3)	
Moderate (1-9 g)	57.9%(62)	54.5%(6)	58.5%(24)	40.0%(6)	0%(0)	
Stiff (≥ 9 g)	6.5%(7)	9.1%(1)	22.0%(9)	33.3%(5)	0%(0)	
Final guidewire						<0.001
Fielder	29.3%(27)	0%(0)	12.5%(5)	57.1%(8)	0%(0)	
Miracle	6.5%(6)	9.1%(1)	5.0%(2)	0%(0)	0%(0)	
Pilot	40.2%(37)	9.1%(1)	15.0%(6)	21.4%(3)	0%(0)	
Gaia	10.9%(10)	27.3%(3)	22.5%(9)	0%(0)	33.3%(1)	
Confianza	7.6%(7)	18.2%(2)	17.5%(7)	0%(0)	0%(0)	
Ultimate	2.2%(2)	0%(0)	2.5%(1)	0%(0)	0%(0)	
Sion	1.1%(1)	9.1%(1)	5.0%(2)	0%(0)	0%(0)	
PT	0%(0)	0%(0)	0%(0)	21.4%(3)	0%(0)	
Gladius	1.9%(2)	9.1%(1)	12.2%(5)	0%(0)	66.7%(2)	
Progress	0%(0)	18.2%(2)	4.9%(2)	0%(0)	0%(0)	
Cross-it	0%(0)	0%(0)	2.4%(1)	0%(0)	0%(0)	
Failed procedure	14.0%(15)	0%(0)	2.4%(0)	6.7%(1)	0%(0)	
Final guidewire type						<0.001
Polymeric	71.7%(66)	18.2%(2)	40.0%(16)	100%(14)	66.7%(2)	
Non-poylmeric	28.3%(2)	81.8%(9)	60.0%(24)	0%(0)	33.3%(1)	
Final wire stiffness						0.001
Soft (<1 g)	29.3%(27)	9.1%(1)	17.5%(7)	64.3%(9)	0%(0)	
Moderate (1-9 g)	57.6%(53)	36.4%(4)	50.0%(20)	35.7%(5)	66.7%(2)	
Stiff (≥ 9 g)	13.0%(12)	54.5%(6)	32.5%(13)	0%(0)	33.3%(1)	
Same initial-final wire	64.5%(69)	9.1%(1)	9.8%(4)	26.7%(4)	0%(0)	<0.001
Total	60.5%(107)	6.2%(11)	23.2%(41)	8.5%(15)	1.7%(3)	

g:gram

P<0.05 is indicated as significant

Table 9. Distribution of first-choice and final crossing guidewires characteristics according to J-CTO score.

Variables	J-CTO 0	J-CTO 1	J-CTO 2	J-CTO 3	J-CTO 4	J-CTO 5	*p*
Guidewire number	3.21±1.57	3.60±1.88	4.87±2.50	6.04±2.05	7.28±4.02	3.0±1.0	<0.001
1-3	73.9%(34)	60.0%(30)	32.7%(16)	8.3%(2)	14.3%(1)	100%(1)	
4-6	21.7%(10)	30.0%(15)	49.0%(24)	54.2%(13)	42.9%(3)	0%(0)	
7-10	4.3%(2)	8.0%(4)	14.3%(7)	33.3%(8)	14.3%(1)	0%(0)	
>10	0%(0)	2.0%(1)	4.1%(2)	4.2%(1)	28.6%(2)	0%(0)	
Initial guide wire							0.12
Fielder	34.8%(16)	24.0%(12)	24.5%(12)	29.2%(7)	0%(0)	0%(0)	
Miracle	4.3%(2)	6.0%(3)	8.2%(4)	4.2%(1)	14.3%(1)	0%(0)	
Pilot	47.8%(22)	44.0%(22)	30.6%(1)	12.5%(3)	28.6%(2)	0%(0)	
Gaia	0%(0)	2.0%(1)	2.0%(1)	8.3.%(2)	0%(0)	0%(0)	
Confianza	2.2%(1)	6.0%(3)	12.2%(6)	29.2%(7)	42.9%(3)	0%(0)	
Ultimate	4.3%(2)	4.0%(2)	12.2%(6)	8.3%(2)	0%(0)	0%(0)	
Sion	2.2%(1)	6.0%(3)	8.2%(4)	4.2%(1)	14.3%(1)	0%(0)	
PT	0%(0)	4.0%(2)	0%(0)	4.2%(1)	0%(0)	100%(1)	
Gladius	2.2%(1)	4.0%(2)	2.0%(1)	0%(0)	0%(0)	0%(0)	
Progress	2.2%(1)	0%(0)	0%(0)	0%(0)	0%(0)	0%(0)	
Initial guidewire type							0.001
Polymeric	84.8%(39)	76.0%(38)	57.1%(28)	45.8%(11)	28.6%(2)	100%(1)	
Non-poylmeric	15.2%(7)	24.0%(12)	42.9%(21)	54.2%(13)	71.4%(5)	0%(0)	
Initial guidewire stiffness							0.02
Soft (<1 g)	34.8%(16)	32.0%(16)	30.6%(15)	33.3%(8)	14.3%(1)	100%(1)	
Moderate (1-9 g)	60.9%(28)	62.0%(31)	55.1%(27)	37.5%(9)	42.9%(3)	0%(0)	
Stiff (≥ 9 g)	4.3%(2)	6.0%(3)	14.3%(7)	29.2%(7)	42.9%(3)	0%(0)	
Final guidewire							0.04
Fielder	32.6%(15)	17%(8)	23.8%(10)	31.6%(6)	16.7%(1)	0%(0)	
Miracle	4.3%(2)	8.5%(4)	2.4%(1)	10.5%(2)	0%(0)	0%(0)	
Pilot	43.5%(20)	38.3%(18)	14.3%(6)	10.5%(2)	16.7%(1)	0%(0)	
Gaia	8.7%(4)	12.8%(6)	21.4%(9)	15.8%(3)	16.7%(1)	0%(0)	
Confianza	6.5%(3)	12.8%(6)	11.9%(5)	10.5%(2)	0%(0)	0%(0)	
Ultimate	4.3%(2)	0%(0)	2.1%(1)	0%(0)	0%(0)	0%(0)	
Sion	0%(0)	2.1%(1)	4.8%(2)	5.3%(1)	0%(0)	0%(0)	
PT	0%(0)	0%(0)	4.8%(2)	5.3%(1)	0%(0)	0%(0)	
Gladius	0%(0)	6.0%(3)	6.1%(3)	8.3%(2)	28.6%(2)	0%(0)	
Progress	0%(0)	2.0%(1)	4.1%(2)	0%(0)	14.3%(1)	0%(0)	
Cross-it	0%(0)	0%(0)	2.0%(1)	0%(0)	0%(0)	0%(0)	
Failed procedure	0%(0)	6.0%(3)	14.3%(7)	20.8%(5)	14.3%(1)	100%(1)	
Final guidewire type							0.15
Polymeric	76.1%(35)	61.7%(29)	50.0%(21)	57.9%(11)	66.7%(4)	0%(0)	
Non-poylmeric	23.9%(11)	38.3%(18)	50.0%(21)	42.1%(8)	33.3%(2)	0%(0)	
Final guidewire stiffness							0.23
Soft (<1 g)	30.4%(14)	21.3%(10)	28.6%(12)	36.8%(7)	16.7%(1)	0%(0)	
Moderate (1-9 g)	63.0%(29)	55.3%(26)	42.9%(18)	42.1%(8)	50.0%(2)	0%(0)	
Stiff (≥ 9 g)	6.5%(3)	23.4%(11)	28.6%(12)	21.1%(4)	33.3%(2)	0%(0)	
Same initial-final wire	71.7%(33)	58%(29)	26.5%(13)	8.3%(2)	14.3%(1)	0%(0)	<0.001
Total	26.0 % (46)	28.2% (50)	27.7%(49)	13.6%(24)	4.0%(7)	0.6%(1)	

J-CTO: Japan registry of chronic total occlusion, g:gram
P<0.05 is indicated as significant

Table 10. Distribution of first-choice and final crossing guidewires characteristics according to Eurocto score.

Variables	E-CTO 0	E-CTO 1	E-CTO 2	E-CTO 3	E-CTO 4	E-CTO 5	*p*
Guidewire number	3.29±1.79	3.61±1.70	5.31±2.57	4.66±3.02	5.42±2.43	7.33±4.16	<0.001
1-3	70.7%(29)	60.0%(33)	27.6%(16)	41.7%(5)	14.3%(1)	0%(0)	
4-6	22.0%(9)	30.9%(17)	46.6%(27)	41.7%(5)	71.4%(5)	66.7%(2)	
7-10	7.3%(3)	9.1%(5)	20.7%(12)	8.3%(1)	0%(0)	0%(0)	
>10	0%(0)	0%(0)	5.2%(3)	8.3%(1)	14.3%(1)	33.3%(1)	
Initial guide wire							0.06
Fielder	31.7%(13)	21.8%(12)	25.9%(15)	41.7%(5)	28.6%(2)	0%(0)	
Miracle	4.9%(2)	5.5%(3)	6.9%(4)	8.3%(1)	0%(0)	33.3%(1)	
Pilot	48.8%(20)	50.9%(28)	22.4%(13)	8.3%(1)	28.6%(2)	0%(0)	
Gaia	2.4%(1)	1.8%(1)	3.4%(2)	0%(0)	0%(0)	0%(0)	
Confianza	2.4%(1)	1.8%(1)	22.4%(13)	16.7%(2)	14.3%(1)	33.3%(1)	
Ultimate	2.4%(1)	5.5%(3)	10.3%(6)	8.3%(1)	14.3%(1)	0%(0)	
Sion	4.9%(2)	5.5%(3)	6.9%(4)	0%(0)	0%(0)	33.3%(1)	
PT	0%(0)	1.8%(1)	1.7%(1)	8.3%(1)	14.3%(1)	0%(0)	
Gladius	0%(0)	5.5%(3)	0%(0)	8.3%(1)	0%(0)	0%(0)	
Progress	2.4%(1)	0%(0)	0%(0)	0%(0)	0%(0)	0%(0)	
Initial wire type							0.001
Polymeric	80.5%(33)	80.0%(44)	50.0%(29)	66.7%(8)	71.4%(5)	0%(0)	
Non-poylmeric	19.5%(8)	20.0%(11)	50.0%(29)	33.3%(4)	28.6%(2)	100%(3)	
Initial wire stiffness							0.01
Soft (<1 g)	34.1%(14)	25.5%(14)	32.8%(19)	50.0%(6)	42.9%(3)	33.3%(1)	
Moderate1-9 g)	61.0%(25)	70.9%(39)	44.8%(26)	33.3%(4)	42.9%(3)	33.3%(1)	
Stiff (≥ 9 g)	4.9%(2)	3.6%(2)	22.4%(13)	16.7%(2)	14.3%(1)	33.3%(1)	
Final guidewire							0.39
Fielder	26.8%(11)	19.6%(10)	26.9%(14)	37.5%(3)	20.0%(1)	0%(0)	
Miracle	7.3%(3)	3.9%(2)	5.8%(3)	0%(0)	20%(1)	0%(0)	
Pilot	43.9%(18)	39.2%(20)	15.4%(8)	12.5%(1)	0%(0)	0%(0)	
Gaia	12.2%(5)	9.8%(5)	21.2%(11)	12.5%(1)	0%(0)	0%(0)	
Confianza	7.3%(3)	13.7%(7)	7.7%(4)	12.5%(1)	20.0%(1)	0%(0)	
Ultimate	2.4%(1)	3.9%(2)	0%(0)	0%(0)	0%(0)	0%(0)	
Sion	0%(0)	2.0%(1)	5.8%(3)	0%(0)	0%(0)	0%(0)	
PT	0%(0)	2.0%(1)	5.8%(3)	0%(0)	0%(0)	0%(0)	
Gladius	0%(0)	3.6%(2)	6.9%(4)	16.7%(2)	14.3%(1)	33.3%(1)	
Progress	0%(0)	1.8%(1)	3.4%(2)	0%(0)	14.3%(1)	0%(0)	
Cross-it	0%(0)	0%(0)	1.7%(1)	0%(0)	14.3%(1)	0%(0)	
Failed procedure	0%(0)	7.3%(4)	10.3%(6)	33.3%(4)	28.6%(2)	33.3%(1)	
Final guidewire type							0.50
Polymeric	70.7%(29)	64.7%(33)	53.8%(28)	75.0%(6)	40.0%(2)	50.0%(1)	
Non-poylmeric	29.3%(12)	35.3%(18)	46.2%(24)	25.0%(2)	60.0%(3)	50.0%(1)	
Final wire stiffness							0.20
Soft (<1 gram)	24.4%(10)	19.6%(10)	36.5%(19)	37.5%(3)	20.0%(1)	0%(0)	
Moderate (1-9 g)	65.9%(27)	60.8%(31)	38.5%(20)	37.5%(3)	40.0%(2)	50.0%(1)	
Stiff (≥ 9 g)	9.8%(4)	19.6%(10)	25.0%(13)	25.0%(2)	40.0%(2)	50.0%(1)	
Same initial-final wire	68.3%(28)	58.2%(32)	24.1%(14)	25.0%(3)	14.3%(1)	0%(0)	<0.001
Total	23.2% (41)	31.1% (55)	32.8%(58)	6.8%(12)	4.0%(7)	1.7%(3)	

Eurocto 6 grup: just 1 patient, , guidewire number 8, initial wire is non-polymeric, stiff, Confianza 9 brand, final wire is polymeric, soft Fielder FC brand
E-CTO: Euro chronic total occlusion,
P<0.05 is indicated as significant

4.7.Multivariate analysis

Univariate and multivariate logistic regression analysis performed to obtain determinants of the crossability of initial guidewire. Procedural technique and J-CTO score was independent predictors of initial guidewire crossability (OR:0.326, CI: 0.199;0.535, p<0.001 and OR:0,363, CI: 0.240;0.550, p<0.001) (Table 11). Initial guidewire type and stiffness also independent predictors of initial guidewire success (OR:5.763, CI: 1.980;16.775, p:0.001 and OR:0,324, CI: 0.149;0.705, p:0.004). Initial guidewire brand did not show significant impact on the crossability of initial-choice guidewire (p:0.26).

Table 11. Multivariate logistic regression analysis for reveal the determinants of the crossability of initial choice guidewire.

Dependant variable:	**Multivariate analysis**		
Same initial-final guidewire	**Odds Ratio**	**95% CI**	***p***
Sex (Male/Female)	0.312	0.112;0.869	0.02
LV EF	0.717	0.314;1.640	0.43
Hypokinesia on cto territory	0.733	0.342;1.570	0.42
J-CTO Score	0.363	0.240;0.550	<0.001
Procedural technique	0.326	0.199;0.535	<0.001
Initial guidewire	0.949	0.866;1.040	0.26
Initial guidewire type	5.763	1.980;16.775	0.001
Initial guidewire stiffness	0.324	0.149;0.705	0.004

LV EF: Left ventricular ejection fraction, J-CTO: Japan registry of chronic total occlusion
P<0.05 is indicated as significant

5.DISCUSSION AND CONCLUSION

Guidewire preference and initial choice is a corner-stone in the coronary CTO interventions. Inadequate choice of guidewires decrease the success rate of the procedure and also, it is associated with prolonged procedural time, excessive use of biomaterials, higher complication rate and suboptimal procedural results (24). The CTO instruments are special and expensive biomaterials (22). Logical and economical use of CTO guidewires would decrease the cost of the procedure which is a remarkable limitation of the CTO procedure in Turkey. Healtcare system is usually working over the goverment insurance system and payment for CTO procedure is same as a simple angioplasty procedure. The total price of new design CTO guidewires even higher than total procedural payment by the goverment insurance in Turkey. Thus, patient should effort the certain percentage of the procedure by themselves. More guidewire usage means higher cost for patients. Herein, we analysed the preference and performance of the CTO guidewires according to clinical and angiographic parameters. This study was the first report from Turkey that analysed the rational guidewire use and procedural success in CTO procedures. We found that, lower number of the guidewire usage is possible especially in easy and moderately difficult CTO procedures. Crossing of the CTO lesion with initial choice guidewire would decrease biaomaterial use and also cost of the procedure. Classification of the CTO lesion by the J-CTO or Eurocto score would lead to more precise strategy. Polymeric jacked moderate tip stiff guidewires, particulary Pilot brand, has a superior crossability in the easy and moderate CTO procedure.

Advances in the biomaterial technology open a new era in percutaneous coronary interventions. Parallel to introduction of more delicate instruments, success rate of the cardiac interventions signally increase to over 90% (22). New technology in the stent production affect the long term patency of the stent in a favorable way. However, success rate of coronary CTO interventions still under the desirable level comparing to Standard procedures. In the most centers, success rate of CTO procedure is below the 80%. Moreover, majority of the patients having CTO lesion are just taking anti-anginal drugs in stead of cardiac interventions. Cardiac CTO procedure necessitate special instruments to increase success rate. Using standard angioplasty materials for CTO intervention often associated with suboptimal result or failed procedure (21). Guidewire choice is crucial step in CTO procedure (26). Forced effort with traditional guidewire usually lead to large dissection in the CTO segment which requires longer stents even full metal jacket. Thus, it is obivious that CTO procedure should be perpormed with special biomaterials (27).

Availibility of CTO spesific biomaterials is usually limiter especially in public hospital. Most centers just belong to a few brands of CTO spesific materials including guidewires, microcatheters and balloon catheters. So, rational use of such biomaterials are important for sustainable CTO interventions.

Each CTO dedicated guidewire has a different tips structure, polymer jacket and tip stiffness (22). Variation in guidewire structure affect the steerability, crossability and tactile feedback of the guidewire. Operators should be familiar with the structure of the guidewires, and then should form a strategy for the technique and guidewire choice (25). Polymer jacked guidewire has a superior steerability, however subintimal course is common and due to limited tactile feedback, operators should use them very carefully (9,12). Non-polymeric guidewires has a better tactile feedback and intra-luminal course. However their seerability is inferiror to poylmeric wires. Stiff tip is important for lesion penetration and wire escalation. Tough stump necessitate more stiff guidewires. Our experince showed that, non-polymeric and stiff guidewires are more commonly preferred in complex lesions. Polymeric guidewires are more useful in easy and intermediate lesion. Presence of microchannel are the optimal indication for soft and moderate stiff tip polymeric guidewires (29).

Lesion characteristics including length, calcification, tortouisity, stump, distal area, occlusion duration, all are important for define an optimal strategy (28,29). Several CTO scores was proposed to determine the successfull CTO procedure (30). In stead of evaluating the lesion characterstics one by one, simpy total CTO score may predict the success rate of the procedure. J-CTO score was developed in the light of Japan Multicenter CTO registry on 2006. It was approved by the following investigations which predict the success rate of antegrade CTO interventions (31). Lower J-CTO score usually accepted as a easy and intermediate difficulty cases. Higher scores indicate very difficult cases. Our procedures was performed mostly by antegrad approach. Thus, J-CTO score is a suitable chart to assess our cases. Aproximately 80% of the patient has J-CTO score 0-2 lesion. So, we can conclude that our results is appropriate to analyse easy, intermediate and difficult cases. Very difficult cases constitude just 17% of the total cases. There was a inverse correlation between J-CTO score and success rate which was in corcondance with medical literature (11,31). All the J-CTO 0 lesion was intervented successfully. There was also an inverse relationship between crossability of the initial guidewire and J-CTO score. More than 50% of the J-CTO 0-1 lesion was crossed with initial guidewire. This statistic reveal the importance of the initial guidewire choice. Reasonable initial wire choice and single wire cross strategy would lead to shorter procedural and fluroscopy time, lower number of guidewires, balloon and stent usage which affect the affordability and long term prognosis. Polymeric and moderate stiff tip guidewires showed superior performance in crossing the CTO segment. Choice of Pilot brand in J-CTO 0-1 lesion would increase the probability of wire cross with initial guidewire. In such lesion type, non-polymeric stiff guidewires should not be used as a initial guidewire.

In each CTO procedure, use of 1-3 guidewires can be accepted as a economical and rational use. In the each procedure a standard soft tipped or polymer jacked guidewire used to place microcatheter. Then, special CTO guidewires replace the initial standard wire for lesion penetration. In the final stage, standard wire exchange with CTO wire once again to perform balloon and stent procedure. Special CTO wire should be used just for lesion penetration. This strategy necessitate at least 2-3 wire for each procedure. In our cases average number of guidewires was lesser than 4 in J-CTO 0 and 1 group. We can conclude that, use of >4 guidewires in antegrade J-CTO 0-1 lesion was not rational and it can be defined as overuse. The crossability of the polymeric soft and moderate tip stiff guidewires is not so good J-CTO>2 lesions. For this more complicated lesion, stiff tip non-polymeric guidewires should be preferred. Gaia brand showed more significant crossability performance in J-CTO >2 lesion. Distribution of the Fielder brand is similar between the all J-CTO group. But, there was a small details in the performance of Fielder guidewires. In the J-CTO 0-1 group, crossability of the Fielder wire as a initial choice is higher and single wire technique was usually preferred. In the more complex cases, other techniques, particularly step up and step down was preferred. Lesion was modified with multiple guidewires including non-polymer stiff guidewires and Fielder wire just used to jump to true lumen. Thus, similar distribution of Fielder brand as a final guidewire does not indicate the strong crossability in J-CTO>2 lesions.

Eurocto score or CASTLE score was defined in the light of prospective Eurocto registry (30). This novel scoring chart was compared with J-CTO score and it was found to be superior in more complex cases. We performed J-CTO score like analysis also for Eurocto score. Our result was comparable for both scoring chart. Eurocto 0-1 groups showed similar result with J-CTO 0-1 group. The average guidewire number was below the 4 and more than 50% of the lesion was crossed with initial guidewire. Polymeric moderate stiff tip guidewires showed superior performance in crossing the CTO segment as an initial choice guidewire. However, final wire brand, composition and stiffness did not differ among to the Eurocto score group. Nonetheless we can state that more stiffer tip guidewires was preferred for higher Eurocto score. As a limitation, Eurocto 5-6 lesions was just 4 which reduce the significant statistical analysis for very complex lesion. Non-polymeric moderate to stiff tip guidewire used more commonly used in the Eurocto 1-4 group as a final guidewire comparing to initial wire type. Our data confirmed that polymeric moderate stiff tip Pilot brand is a good choice for Eurocto 0-1 lesion.

Our result strongly confirmed that use of CTO scoring chart would influence our technique in a favorable way which directly affect the initial guidewire choice. Single wire escalation is associated with less guidewire usage. For the easy and intermediate CTO lesion, single wire crossing should be initial choice for rational guidewire usage. Other tecniques including parallel wire, step up-step down and dissection re-entry associated with very low probability of penetration of the lesion with initial guidewires. However, parallel wire techique offer more rational guidewire use. Average number of guidewire use is lower comparing to step up – step down and dissection re-entry techniques. Polymeric guidewires are more successfull in the single wire escalation. Non-polymeric guidewires should be chosen in the other techniques. According to lesion modification during the wire escalation and drilling, optimal guidewire exchange should be performed. For the dissection and re-entry technique, polymeric guidewires should be preferred to jump into true lumen.

Use of new generation guidewire would increase the success rate. However affordability of the new generation guidewire would limit their optimal preference. Fielder brand is one of the most common preferred soft polymeric guidewires. They have a tapered soft tip structure which temper their crossability. We usually preferred Fielder XT series rather than new generation Fielder XT-A. This choice may overshade the crossability of Fielder brand. New generation Fielder XT-A series have an additional composite core technology in the guidewire tip which enhance the crossability. We used just Fielder XT-A series onl in 4 cases which did not show statistical significant superiority. On the other hand, new generation non-polymeric guidewires are preferred more comparing to older series. Miracle brand is a well-known non-polymeric guidewire of Asahi Intecc. New generation Gaia brand with composite core technology replaced the Miracle series. In our experince, Gaia brand preferred more than Miracle series which would directly affect the success rate. On the other hand, we used first generation Gaia 1-2-3 brand. New-released Gaia next series which has xtrand coil technology did not used in any cases. For more complex lesion which necessitae stiff tip load, Confianza 9 was preferred rather than

Confianza pro series which possess thinner tip and more slippery hydrohilic coating. Moreover, we also used Gladius guidewire as a last resort in certain cases. Gladius brand is new generated peripheral guidewire which has a durable balanced tip composition. It has relatively superior crossability for intermediate and difficult lesion. Although it is designed for peripheral interventions, it can be used for coronary CTO procedure in selected cases as a rescue solution. On the other hand, new coronary series of Gladius MG guidewire did not used due to unavailibility.

Preferance of new generation guidewires would lead to more successfull procedural results. However, the experience of the operator also as important as technology (32). Our case series, new released guidewires was used in a few cases. Nonetheless, our procedural success rate is above the average (aproximately 90 %). Each operators have a special relationship with guidewires and each has their different favorite wires for different occasion. Experienced operators predict the behavior of the guidewire in each different lesion composition. Indeed, all operators want to perform CTO procedure with new released technology. Unfortunately it is not possible in most cardiac center located in Turkey. For this reason, operator should know the composition and behaviour of the all guidewire brands to choice guidewires in a rational manner.

In the other hand, crossing of the CTO lesion rarely does not end up with successfull procedure. Such a lesions usually described as balloon uncrossable lesion (33). In such circumstance, use of dedicated supportive devices like new generation balloon catheters, microcatheters, debulking techniques would increase the success rate of the procedure. In our sample, 3 cases could not finalized with stent deployment although lesion was crossed with guidewires (17% of the failed procedure). Thus use of new biotechnology in the all instruments dedicated for CTO interventions is important for successful procedure.

5.1.Future Perpectives

Recent advance in medical biotechnology lead to manufacturing of the more smart coronary guidewires which directly affect the procedural success of CTO interventions. Majority of the innovations performed in the tip structure of the guidewires which directly face with the CTO lesion. Additional features may be incorporated into tip structure in the near future. Definitive analysis of the CTO lesion is essential to build an optimal strategy. Simple contrast injection usually is not enough to assess the lesion characteristics. Computed tomography (CT) and intra vascular ultrasonography (IVUS) are the two frontier method to analyse CTO lesion (34-35). In pre-procedural analysis, CT scan may give important information about the CTO lesion, particulary extent of the calcification, bending and coursing of the vessel. However, intra-procedural use of CT scan is not available in the most cardiac centers. Intravascular ultrasonography is the most common imaging technique using during the coronary interventions. It gives clues about side branch, true lumen and complication like dissection and hematoma formation. Contemporary use of IVUS may influence the intraluminal escalation of the guidewire more precisely (36). Current IVUS wires has a delicated tip structure and they are not suitable for lesion penetration. A dedicated CTO wires with IVUS feature would be a pioneer in the CTO interventions. Moreover, using of the sound wave for lesion modification is an another innovation in coronary interventions (37). Modification and breaking of the calcific plaques with sound waves is associated with better procedural results and it also affect prognosis in a favorable way. Balloon catheter is currently using for shock wave generation. Addition of the the shockwave feature to CTO dedicated guidewire would give an excellent results especially in the calcific and balloon uncrossable lesion. This innovations were initially experinced in the lower extremity lesion which gave a promising results (38-39). However, mounting of the shockwave technology to CTO dedicated guidewires would take a more time to use in the clinical practice.

5.2.Limitations

First limitation is a relatively small number of the sample. For assessing new released biotechnology we analysed the recent past period of time. So, our case sample is relatively small but it is over the initial thesis project (150 cases). Retrospective manner of the analyses could be questioned. However, all the cases was retrieved from the CTO registry in which cases was followed prospectively. Thus, our analysis could be defined as cross-sectional observational study. All the the procedure was performed by the same CTO teams which arise a question about the personal preference of the guidewires. Although, procedures was performed by the same team, the cases was collected from the different hospitals which has their own catheter laboratory working and independent purchasing department. So, the CTO operators preferred the guidewire according to availibility in the catheter laboratory.

5.3.Conclusion

Adequate strategy and logical guidewire choice are the key for successfull CTO interventions. There is a brilliant development in CTO dedicated guidewire biotechnology and new genereations of the guidewires are releasing frequently. CTO operators should follow all the new biotechnologic innovation and they should be familiar with the composition and behavioral characteristics of the guidewires. On the other hand, innovations and new released biomaterials are usually expensive and their clinical usage is under the desired level. In stead of experience a new technology, most of the operators continue to preferred their usual known biomaterial. In this investigations, we analysed the rational use of coronary CTO guidewires. Although success rate of the procedures was higher, use of new released guidewire was relatively limited. This result showed that, it would take a time to get use the new released biomaterials in clinical practice. Affordability is a major limitation for CTO instruments. Total cost of the procedure could be as higher as 20 times of standard procedure. Rational use of CTO guidewire could decrease the total use of biomaterials and also decrease the procedural time and complication rate. Lesion characteristics are the most important factor for generating a succesfull strategy. Classification of the lesion by J-CTO score and Eurocto score would influence the choice for strategy and guidewire preference. In the J-CTO 0-1 and Eurocto 0-1 lesion, single wire crossing techniques were associated with a fewer guidewire usage. Most of the such lesion could be crossed by the initial guidewires. Polymeric, moderate stiff tip guidewires, particularly Pilot brand, have a superior crosability as a initial guidewire. Penetration of the lesion with initial guidewires would bring down the average guidewire use below the 4. Same initial-final wire strategy also predict the less balloon number, shorter stent length, shorter fluroscopy duration and less amount of contrast use. However, same initial-final wire strategy is not successful in difficult and very difficult lesions (J-CTO>2, Eurocto>2). In such group new innovative non-polymeric guidewires particulary Gaia brand seem to be superior in lesion penetration. Off-label use of innovative biomaterials could be helpful in selected patients as a last resort. Gladius brand which dedicated for peripheral vascular interventions could be a rescue choice in difficult and very difficult CTO lesions. New generation guidewires usually developed according to demands of certain clinician. They are not only an engineering marvel. Their clinical test performed in certain laboratory before release of the biomaterials. Thus, every operators should insist to use new biotechnology in clinical circumferences. Real world data feedbacks are important for modifiying the new medical product to reach a final intended perfection.

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7.APPENDIX

Appendix 1: Report of the Ethics Committee

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8.CURRICULUM VITAE