Intracavitary electrocardiography for tip location during central venous catheterization: A narrative review of 70 years of clinical studies

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Abstract
Intracavitary electrocardiography is an accurate and non-invasive method for central venous access tip location. Using the catheter as a traveling intracavitary electrode, intracavitary electrocardiography is based on the increase in the detected amplitude of the P wave while approaching the cavoatrial junction. Despite having been adopted diffusely in clinical practice only in the last years, this method is not novel. In fact, it has first been described in the late 40s, during electrophysiological studies. After a long period of quiescence, it is in the last two decades of the XX century that intracavitary electrocardiography became popular as an effective mean of central venous catheters tip location. But the golden age of this technique began with the new millennium, as documented by high-quality studies in this period. In fact, in those years, intracavitary electrocardiography has been studied broadly, and important achievements in terms of comprehension of the technique, accuracy, and feasibility of the method in different populations and conditions (i.e. pediatrics, renal patients, atrial fibrillation) have been gained. In this review, we describe the technique, its history, and its current perspectives.

Keywords
Intracavitary electrocardiography, tip location, tip navigation, central venous access, catheter-related complications, central venous access devices

Introduction
The correct position of the tip of central venous access devices (CVADs) is essential in order to avoid catheter-related complications such as malfunction, thrombosis, vascular and valve erosions, or arrhythmias. Intracavitary electrocardiography (IC-ECG) is a non-invasive, safe, inexpensive, and accurate method for intraprocedural verification of the correct position of the tip. First described by Hellerstein et al.⁴ in 1949, its early use as a method for tip location is dated back in the 60s in the field of neuroanesthesia, with a subsequent exponential development only in the last 20 years. The year 2019 marked the 70th anniversary of the first study about IC-ECG.

Short description of the technique of IC-ECG
The IC-ECG method is based on the use of the catheter tip as a “travelling intracavitary electrode.” The vector of the lead II of ECG is approximately co-axial to the vector of the atrial depolarization, so that—when one of the two electrodes of lead II is moving inside the superior vena cava (SVC)—the ECG trace shows a progressive increment of the height of the P wave, reaching the maximal positivity as the intracavitary electrode gets to the cavoatrial junction (CAJ), that is, when all the depolarized atrial mass is in front of the electrode. Advancing the catheter further into the right atrium (RA), the P wave becomes biphasic (negative/positive); at this point, the catheter tip

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(which we use as intracavitary electrode) can be withdrawn to the previous point of maximum P positivity—if the desired position is at CAJ—or left where the P is biphasic, if the desired position is in the atrium.

The catheter tip can be used as “intracavitary electrode” by two different methods: the “metal guidewire” method or the “column of saline” method. With the first method, a metal guidewire is inserted into the catheter so that the distal end reaches and slightly goes past the catheter tip, while the proximal end is connected to the right shoulder electrode, either directly via the ECG clamp or indirectly through a special connector (depending on the choice of the manufacturer). The second method—which has gained greater popularity because it is easier to perform and applicable to any CVAD—is based on the observation that when the catheter is filled with saline solution, its conductivity is optimal. Since the walls of the catheter are made of isolating material, when the saline inside the catheter is connected with the right shoulder electrode through an appropriate transducer, the voltage inside the saline solution will be comparable to the voltage at the open end of the catheter.

History of IC-ECG in the medical literature

Prehistory

Based on the electrophysiological studies previously conducted by Battro and Bidoggia and Heeth, in 1949, Hellerstein et al. showed how a central venous catheter could record an IC-ECG. Electrical connection was achieved by means of a post-procedural CXR. A few years later, Corsten et al. and Calabuig et al. came to the same conclusion, even suggesting that when the P wave is clearly visible on IC-ECG, further control by chest X-ray (CXR) may not be required. Most studies of the XX century suggested that the metal guidewire might be preferred over the column of saline. Also, practically all of these studies verified the accuracy of IC-ECG for tip location by means of a post-procedural CXR. However, what emerged from these studies was clear: the technique was accurate, easy to perform, and above all, inexpensive. Nonetheless, in this period, the clinical use of IC-ECG for tip location was mainly limited to a few European hospitals (particularly in Germany, Belgium, Austria, and Italy).

The golden age of IC-ECG

With the beginning of the new millennium, we entered the so-called “golden-age” of IC-ECG. In 2004, Pawlik et al. compared the guidewire and column of saline techniques, suggesting that the guidewire technique was better in terms of quality of ECG recording, being comparable in terms of accuracy, while the risk of arrhythmias related to the introduction of the wire into the right atrium seemed minimal. A few years later, in 2011, Kremser et al. designed a similar study, finding that, while for catheterization on the right side, there was no significant difference in accuracy between the two techniques, but when the CVAD was inserted on the left side, the guidewire method yielded an underestimation of the length of the catheter.

At the beginning of the XXI century, IC-ECG was investigated more closely. In a few interesting studies, Schummer and colleagues described three possible pitfalls of the technique: (a) IC-ECG is not able to detect accidental intra-arterial positioning of the catheter; (b) during insertion of CVADs on the left side, P wave may sometimes increase before reaching CAJ; in particular, this occurs with the guidewire method, as the metal guidewire touches the lateral wall of the SVC, where this vein is wrapped in the pericardial reflection; and (c) IC-ECG cannot discriminate an extravascular placement of the catheter, as the one resulting from vessel perforation. The current methods of ultrasound guided venipuncture, ultrasound-based tip navigation, and correct interpretation of the changes of the P wave pattern have minimized the clinical relevance of these pitfalls.

In 1992, Francis et al. found a clear advantage of IC-ECG versus “blind” tip location (96% of success vs 59%). A few years later, Corsten et al. and Calabuig et al. came to the same conclusion, even suggesting that when the P wave is clearly visible on IC-ECG, further control by chest X-ray (CXR) may not be required. Most studies of the XX century suggested that the metal guidewire might be preferred over the column of saline. Also, practically all of these studies verified the accuracy of IC-ECG for tip location by means of a post-procedural CXR. However, what emerged from these studies was clear: the technique was accurate, easy to perform, and above all, inexpensive. Nonetheless, in this period, the clinical use of IC-ECG for tip location was mainly limited to a few European hospitals (particularly in Germany, Belgium, Austria, and Italy).
Using TEE imaging, IC-ECG patterns of the different explorable areas were finally described with precision: (a) a normal P wave identifies a position in the upper portion of the SVC, (b) a growing P wave identifies a position in the lower portion of the SVC, (c) the maximum peak of the P wave identifies exactly the CAJ, and (d) a biphasic P wave identifies the entry into RA.

In addition, Ender found that the tip of peripherally inserted central catheters (PICCs) inserted via basilic or axillary veins can move even 3–4 cm during arm movement,31,32 while the tip of centrally inserted venous catheters (CICCs) inserted in the right internal jugular vein does not move more than 1 mm with head movements.

In 2007, the first randomized controlled trial on IC-ECG was published: in 290 patients, Gebhard et al.33 showed that the CVAD tip was correctly positioned at postoperative CXR in 96% of the IC-ECG group versus 76% of controls. Also, they found an intra-atrial or intraventricular placement of the tip of the CVAD in 10% of controls versus none in the study group. The authors concluded emphasizing the safety of IC-ECG, as well as the reduction of costs associated with the decreased need for repositioning.

Between 2008 and 2010, the first studies specifically focused on using IC-ECG during PICC insertions were published. Pittiruti and coworkers34 published a comparison study with CXR, followed by Moureau et al.,35 both studies demonstrated the feasibility and the accuracy of IC-ECG for PICC insertions, pointing out that, since pleuropulmonary complications were virtually impossible after PICC insertion, post-procedural control with CXR would become unnecessary. As stated in a review published a few years later:36 “the IC-ECG method removes the need for post-procedural CXR if there is no expected risk of pleuropulmonary damage to be ruled out (i.e. any kind of PICC; US guided central venipuncture).”

In 2009, the ESPEN (European Society of Parenteral Nutrition) guidelines were the first international guidelines to recommend the use of IC-ECG for tip location, stressing the wide range of applicability, feasibility, safety, and accuracy of IC-ECG in pediatric patients. IC-ECG can be applied in UVC and in ECC, in children. The first clinical experiences in this area are very old (XX century) and they can be traced in Russia,54 Italy,55,56 Canada,57 Germany,58–60 the United States,61 Spain,62 and France.63 Many more studies have been published in XXI century,64–68 some of them dealing specifically with UVC69 or with ECC.70–72 In 2015, the first multicenter study on IC-ECG in pediatrics was published,73 and in the same year the AIEOP (Italian Association of Pediatric Hematology and Oncology74) guidelines recommended that in children “tip location should be ideally verified in real time during the procedure (by fluoroscopy, by intracavitary electrocardiography or by echocardiography)—as a second option—soon after the procedure (by chest x-ray or by echocardiography).” All of these studies demonstrated the wide range of applicability, feasibility, safety, and accuracy of IC-ECG in pediatric patients. IC-ECG can be applied in UVC and in ECC, though there might be some technically issues related to the small caliber of ECC (the column of saline inside catheters <3Fr may have a lower conductivity).74 The use of IC-ECG for tip location of ECC and UVC may be limited by the observation that ultrasound-based tip location by transthoracic echocardiography (TTE) is particularly easy and accurate in neonates; thus, in this setting, CXR (less accurate, more expensive, and less safe) will eventually be replaced by TTE rather than by IC-ECG.74 However, for CICCs ≥3Fr in neonates and for all CVADs in children, IC-ECG is the ideal tip location method, being simpler than...
TTE, but safer, more accurate, and less expensive than CXR or fluoroscopy.

**IC-ECG in nephrology**

Another specific field of application of IC-ECG has been the placement of CVADs for dialysis. The first clinical studies in this area came mainly from Italy,²⁵–⁸⁰ and more recently from some non-Western countries.⁸¹,⁸² All of these studies showed consistently that the IC-ECG is easy, inexpensive, and accurate also for dialysis catheters. The main advantage of IC-ECG for dialysis catheters is the possibility of comparing the ECG tracing between the two lumens, even long time after insertion. Although, the accuracy of IC-ECG may be limited when one lumen has different holes located at different distances from the tip.

**IC-ECG coupled with tip navigation**

All of the previous studies have investigated IC-ECG as a method for tip location. At the appearance of the first ECG monitors specifically dedicated to the IC-ECG technique, some of them were equipped with the special feature of coupling the ECG-based tip location with some methods of tip navigation. Although, the association between IC-ECG and doppler-based navigation,⁸³–⁸⁶ as well as between IC-ECG and electromagnetic navigation,⁸⁷–⁹¹ does not seem to yield significant advantages if compared to IC-ECG alone in terms of cost-effectiveness. In particular, should tip navigation be required, ultrasound-based tip navigation is more accurate, easier, and more cost-effective than electromagnetic tip navigation.⁹²

**IC-ECG in atrial fibrillation**

Very recently, the possibility of adapting the IC ECG methods to patients with atrial fibrillation (AF), who have no detectable P wave, has also been addressed. This was a relevant limitation of IC-ECG, considering that AF is present in 7%–11% of the hospitalized patients.⁹³–⁹⁵ In a study conducted in 1989, Engelhardt et al.⁹⁶ hypothesized that, in AF patients, the highest level of electrical activity detected in the TQ tract could be a valid surrogate of the P wave, thus identifying the CAJ. The rationale for this assumption is that the depolarization of the atrium in AF is represented by the so-called “f” waves, a cluster of irregular waves clearly visible in the TQ tract. In other words, in this “modified” IC-ECG method, the “f” waves should be used as surrogate of the P wave. This finding was confirmed by more recent reports,⁹⁷,⁹⁸ but none of these were conclusive, since this “modified” IC-ECG technique was compared with CXR, which is not the most accurate method of tip location.

In 2018, Calabrese et al.⁹⁹ could finally verify the accuracy of the modified IC-ECG method in AF patients using TEE as reference. An IC-ECG trace was recorded with the catheter tip at three different positions identified by TEE: in the SVC (2 cm above the CAJ); at the CAJ; and in the RA (2 cm below the CAJ). This study demonstrated that a “modified” IC-ECG method based on the maximal electrical activity of the TQ tract (i.e. the height of the “f” waves) could accurately detect the location of the tip of CVADs in AF patients. The authors concluded,⁹⁷ “modified IC-ECG should replace other tip location methods currently used in AF patients, such as fluoroscopy or post-procedural chest x-ray, since such radiological techniques are less accurate, more expensive and less safe than IC-ECG.”

**Current perspectives**

The correct location of the tip of CVAD is of paramount importance and should be verified before starting any intravenous infusion. Although both post-procedural and intra-procedural methods for tip location exist, the latter should be preferred, since they are more accurate, more cost-effective, and they allow immediate initiation of infusion therapy, avoiding the risks and costs of catheter repositioning.²

After its first description in 1949, the IC-ECG method has been studied and brought into clinical practice in the XX century, and it is now becoming more and more popular in the XXI century. After decades of clinical studies, the evidence of its accuracy, safety, and cost-effectiveness has become so strong that current guidelines recommend it as the method of choice for CVADs tip location.² In fact, among the intra-procedural methods, IC-ECG has demonstrated many advantages. If compared to fluoroscopy, it is more accurate, simpler, safer, more readily available and more cost-effective. If compared to TTE, it is simpler and requires less training. The main theoretical advantage of TTE over IC-ECG is its wider applicability, since the electrocardiographic finding is not affected by disturbances of the cardiac rhythm.¹⁰⁰ Quite recently, a modified version of the IC-ECG technique has been developed for AF patients, and it appears to be applicable, feasible, and accurate; though, in a small minority of cases—typically in non-AF cardiac patients where the P wave might be difficult to identify for different reasons—both the standard IC-ECG and the “modified” IC-ECG cannot be applied, and TTE may be the only choice for an accurate, safe, intra-procedural tip location.

In conclusion, while the role of radiology for tip location of CVAD is inevitably becoming more marginal, the next challenge will be the appropriate definition of the advantages and disadvantages of IC-ECG versus TTE in different clinical situations and different CVADs.

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