International Journal of Technology Assessment in Health Care

cambridge.org/thc

Assessment

Cite this article: Thivilliers A-P *et al* (2020). The learning curve in transcatheter aortic valve implantation clinical studies: A systematic review. *International Journal of Technology Assessment in Health Care* **36**, 152–161. https://doi.org/10.1017/S0266462320000100

Received: 15 May 2019
Revised: 21 January 2020
Accepted: 6 February 2020
First published online: 21 April 2020

Key words:
Transcatheter aortic valve implantation; Percutaneous valve; Learning curve; Roll-in; Systematic review

The learning curve in transcatheter aortic valve implantation clinical studies: A systematic review

Anne-Pauline Thivilliers[1], Rémi Ladarré[1], Océane Merabti[1], Caroline François[1], Sarah Fontenay[1], Hélène van den Brink[3], Judith Pineau[1], Patrice Prognon[1], Isabelle Borget[2,3] and Nicolas Martelli[1,3]

[1]Pharmacy Department, Georges Pompidou European Hospital, AP-HP, 20 Rue Leblanc, 75015 Paris, France; [2]Department of Health Economics, Gustave Roussy Institute, 114, Rue Edouard-Vaillant, 94805 Villejuif, France and [3]Faculty of Pharmacy, University Paris-Sud, GRADES, 5 Rue Jean-Baptiste Clément, 92290 Châtenay-Malabry, France

Background. Transcatheter aortic-valve implantation (TAVI) has become an essential alternative to surgical aortic-valve replacement in the treatment of symptomatic severe aortic stenosis, and this procedure requires technical expertise. The aim of this study was to identify prospective studies on TAVI from the past 10 years, and then to analyze the quality of information reported about the learning curve.

Materials and methods. A systematic review of articles published between 2007 and 2017 was performed using PubMed and the EMBASE database. Prospective studies regarding TAVI were included. The quality of information reported about the learning curve was evaluated using the following criteria: mention of the learning curve, the description of a roll-in phase, the involvement of a proctor, and the number of patients suggested to maintain skills.

Results. A total of sixty-eight studies met the selection criteria and were suitable for analysis. The learning curve was addressed in approximately half of the articles ($n = 37$, 54 percent). However, the roll-in period was mentioned by only eight studies (12 percent) and with very few details. Furthermore, a proctorship was disclosed in three articles (4 percent) whereas twenty-five studies (37 percent) included authors that were proctors for manufacturers of TAVI.

Conclusion. Many prospective studies on TAVI over the past 10 years mention learning curves as a core component of successful TAVI procedures. However, the quality of information reported about the learning curve is relatively poor, and uniform guidance on how to properly assess the learning curve is still missing.

In the treatment of symptomatic severe aortic stenosis (AS), transcatheter aortic-valve implantation (TAVI) has become an essential alternative to surgical aortic-valve replacement (SAVR) for patients with severe AS who are either inoperable or at high risk for SAVR (1–3). This technique involves insertion, through a catheter, of a bioprosthetic valve, which is implanted within the patient's diseased aortic valve (1). Through both progressive improvement in TAVI device design and increasing experience of interventional cardiologists, complications arising from TAVI have decreased (4).

However, to achieve optimal procedural performance, interventional cardiologists using TAVI require training and accumulation of experience. Indeed, several studies have suggested that TAVI procedures are technically complex and have a significant learning curve (5–8). In a trial report on a medical device by Motte et al., it appears essential to know how the learning curve was evaluated or how the training of operators was managed (9). A minimum amount of training for each operator is required to complete this learning curve, as well as carrying out a minimum number of procedures per year to maintain TAVI competency. There seemingly is no consensus on these minimum numbers, and no standardized guidelines when initiating a TAVI program currently exist. Some studies have stated that a minimum of twenty procedures is required to achieve a good level of practice (10). Training protocols are usually based on the participation of experienced proctors, dry laboratory sessions, or animal models (11). The French National Health Authority has suggested that carrying out two procedures per month was the minimum needed for each operator to maintain this technical competency (12;13).

With this in mind, medical device studies, including those regarding TAVI devices, require acknowledgment of a "roll-in" phase to account for the operator learning curve. A roll-in phase can be defined as a training phase, in which an operator uses an investigational medical device for an initial period on subjects enrolled in the study. The number of roll-in subjects is usually limited, and data are not included in the final analysis. In a trial report on TAVI, it clearly appears important to know how the training of the operators was managed. Indeed, it may be difficult to establish the external validity of the study, also called generalizability, without this information (9). In addition, if the roll-in phase is not conducted adequately, an insufficient training regime may lead to an increase in adverse events that are caused by operator error (14). Thus, the quality of a clinical report, that is, providing information about the design, conduct, and analysis of the trial, is evidently separated from the methodological quality of the trial. To our knowledge, there are no studies on the quality of learning-curve reporting either in medical device studies in general or specifically on TAVI. In addition, as the expansion of indications for TAVI is now being suggested—for example in patients who are deemed to be at intermediate risk for surgery—it seems apt to study how information on the learning curve is reported in TAVI studies (15). The aim of the present systematic review was to identify prospective studies on TAVI over the past 10 years, then to analyze the quality of information reported about the learning curve and finally to strengthen the health technology assessment of TAVI by improving the reporting of an essential aspect of device evaluation.

Materials and Methods

Study Selection

This systematic review was performed following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Supplementary File 1). A study protocol was also established to clarify the review and to expose eligibility criteria (Supplementary File 2). The systematic search was performed using PubMed and EMBASE to collect studies regarding the learning curve in a TAVI context. The study protocol specifies the search terms used (Supplementary File 2). Limits were defined on publication date, language, and study design. The focus was narrowed to French or English prospective studies published between 2007 and 2017. We limited our search to 10 years, between 2007 and 2017, because TAVI devices were not launched on the market until 2007. Two independent reviewers screened titles and abstracts to exclude irrelevant or duplicate articles. Exclusion criteria of the articles identified were: not in English or French; not based on the source study; other study designs (i.e., not a prospective study); other subjects (not dealing with TAVI or not on TAVI alone); adverse event reporting; biomarker study; drug study; medical imaging study; or outcome monitoring study. Then, a full-text review was performed on the included articles with the same exclusion criteria as that applied to the title and abstract.

Data Analysis

Publications were first exported to Zotero V4.0.29.15 (2017), and as a second step, exported to Microsoft Office Excel® 2010. Then, a data extraction worksheet was developed in Microsoft Office Excel® 2010 to standardize data extraction and analysis. Various information was collected: first author, year of publication, country of origin, source study, study design (randomized/controlled study, comparative study, single-center, multicenter, and so on), brand name of TAVI, access type of TAVI, number of patients, author being a proctor, center type, and source of funding. To our knowledge, there are no international guidelines for the reporting of learning curve information in clinical studies on medical devices. Consequently, we developed our own checklist to assess the quality of information reported about the learning curve. This checklist is based on the literature on this topic. First, after a first reading of every article retrieved, we checked whether the term "learning curve" was mentioned in the study. Then, based on the work of Raman et al. (16), we reported where "learning curve" was mentioned in the study (introduction, methods, results, or discussion). The location in the text is an important element to consider. Indeed, if the learning curve is mentioned in methods or results, it is likely that the learning curve was anticipated and/or evaluated in the study. As stated by Raman et al., when the learning curve is mentioned only in the discussion, most authors described this point only as one of the factors influencing outcomes of the procedures, which is informative but rarely enough to fully appreciate the learning curve itself. We also considered in our analysis the linked articles (methodological references). Then, we searched for whether a proctorship was mentioned. We also allowed for other terms for "proctor" being used, such as "mentor" or "supervisor." Arai et al. showed that an expert tutoring is likely to reduce the complication and mortality rates in patients undergoing transfemoral-TAVI owing to the effect on the operator's learning curve (17). We checked whether a roll-in phase was mentioned (14). As stated in the Introduction, this phase is essential to improve the operator's skills. When a roll-in phase was stated, we also searched the number of patients treated during this phase and/or whether training on animals was performed. Finally, we also searched for whether the number of patients to maintain skills was mentioned. This information is important to consider because it may greatly influence clinical outcomes when the technique is routinely used. The French National Health Authority recommends a minimum of two procedures per month to maintain skills with TAVI (13). The more a study included information for the learning curve checklist, the more informative it was considered. These data were reported into a Microsoft Office Excel® 2010 worksheet. Then, data from article characteristics and learning curve were combined for the analysis.

Results

Study Selection

After removing duplicates, 764 studies were identified, of which 693 were excluded on the basis of the content of their titles and abstracts. Seventy-one studies were considered in their entirety, following which a further fifteen were then excluded. We focused only on primary research articles, and twelve studies corresponding to methodological references from articles initially extracted were added to the review. Thus, a total of sixty-eight studies met the selection criteria and were suitable for complete analysis (Figure 1).

Characteristics of Included Studies

The details of the included sixty-eight studies are presented in Supplementary Table 1. There was a small increase in the number of studies published between 2006 (before 2007, for studies corresponding to methodological references from articles initially extracted) and 2009, which steadily increased between 2010 and 2012 and fell in 2013; numbers rose to previous levels in 2014 before declining again from 2015, with a little recovery in 2017 (Figure 2).

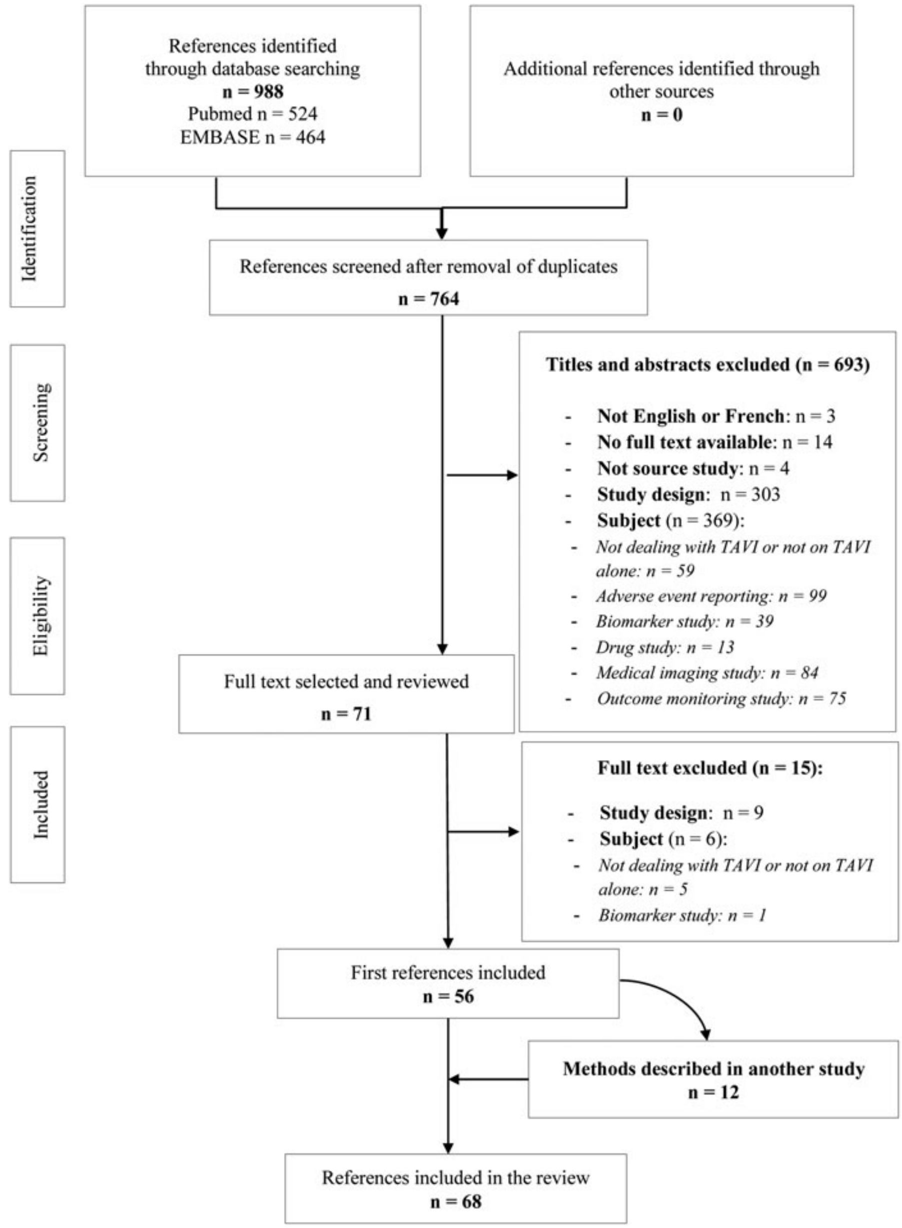

Figure 1. PRISMA flow chart of the included studies.

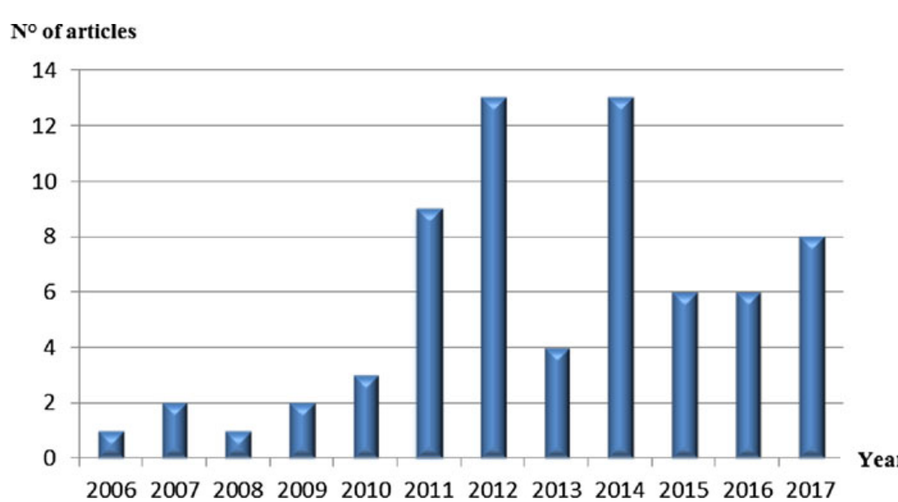

Figure 2. Number of publications per year.

https://doi.org/10.1017/S0266462320000100 Published online by Cambridge University Press

Table 1. Learning curve data extracted from the included studies

Study No.	Author	Year of publication	Number of patients	Roll-in patient	Proctor	Author proctor	PMS	PMS number	Learning curve mentioned in the article (location in the text)
1	Leclercq et al. (21)	2017	240	N	N	N	N	NS	N
2	Deeb et al. (22)	2017	227	N	N	Y	N	NS	N
3	Musa et al. (23)	2017	98	N	N	Y	N	NS	N
4	Greenbaum et al. (24)	2017	100	N	Y	Y	N	NS	Y (discussion)
5	Attizzani et al. (25)	2017	2,069	N	N	Y	N	NS	Y (discussion)
6	Sinning et al. (26)	2017	173	N	N	Y	N	NS	Y (discussion)
7	D'Ancona et al. (27)	2017	118	N	N	Y	N	NS	Y (discussion)
8	Conte et al. (28)	2017	166	N	N	N	N	NS	N
9	Eidet et al. (29)	2016	64	N	N	N	N	NS	N
10	Ahn et al. (30)	2016	60	N	N	N	N	NS	Y (introduction; discussion)
11	Deeb et al. (31)	2016	750	N	N	Y	N	NS	Y (discussion)
12	Thyregod et al. (32)	2016	487	N	N	Y	N	NS	N
13	Barbanti et al. (33)	2016	377	Y	N	N	N	NS	Y (discussion)
14	Ribera et al. (34)	2015	231	N	N	N	N	NS	N
15	Muneretto et al. (35)	2015	163	N	N	N	N	NS	N
16	Pascual Calleja et al. (36)	2015	160	N	N	N	N	NS	N
17	Popma et al. (37)	2014	506	N	N	N	N	NS	Y (discussion)
18	Fanning et al. (38)	2014	80	N	N	Y	N	NS	N
19	Schofer et al. (39)	2014	100	Y	N	Y	N	NS	N
20	Webb et al. (40)	2014	150	N	N	Y	N	NS	Y (discussion)
21	Wendt et al. (41)	2014	8	N	N	Y	N	NS	N
22	Barbanti et al. (42)	2014	1,376	N	N	N	N	NS	N
23	Kasel et al. (43)	2014	185	Y	N	Y	N	NS	Y (discussion)
24	Sawa et al. (44)	2014	55	N	N	N	N	NS	Y (discussion)
25	Hong et al. (45)	2014	59	N	N	N	N	NS	Y (introduction)
26	Fiorina et al. (46)	2014	100	N	N	Y	N	NS	Y (discussion)
27	Reinöhl et al. (47)	2013	60	N	N	N	N	NS	N
28	Gotzmann et al. (48)	2013	202	N	N	N	N	NS	N
29	Kempfert et al. (49)	2013	40	N	N	N	N	NS	Y (discussion)
30	Treede et al. (50)	2012	67	N	N	N	N	NS	Y (discussion)
31	Osnabrugge et al. (51)	2012	546	N	N	N	N	NS	Y (discussion)

(*Continued*)

Table 1. (*Continued.*)

Study No.	Author	Year of publication	Number of patients	Roll-in patient	Proctor	Author proctor	PMS	PMS number	Learning curve mentioned in the article (location in the text)
32	Jegaden et al. (52)	2012	23	N	N	N	N	NS	N
33	Yamamoto et al. (53)	2012	136	N	N	N	N	NS	Y (discussion)
34	Walther et al. (54)	2012	150	N	N	N	N	NS	Y (discussion)
35	Takagi et al. (20)	2011	79	Y	N	N	N	NS	Y (introduction; results; discussion)
36	Walther et al. (55)	2011	168	N	N	N	N	NS	Y (discussion)
37	Modine et al. (56)	2011	17	N	N	Y	N	NS	N
38	John et al. (57)	2010	100	N	N	Y	N	NS	Y (discussion)
39	Krane et al. (58)	2010	99	N	N	N	N	NS	N
40	Clavel et al. (59)	2009	150	N	N	Y	N	NS	N
41	Grube et al. (60)	2008	136	N	N	Y	N	NS	Y (introduction; discussion)
42	Wöhrle et al. (61)	2016	235	N	N	N	N	NS	N
43	Gooley et al. (62)	2015	100	N	Y	N	N	NS	N
44	Kapadia et al. (63)	2015	179	N	N	N	N	NS	N
45	Reardon et al. (64)	2014	150	N	Y	N	N	NS	Y (discussion)
46	Spethmann et al. (65)	2014	99	N	N	N	N	NS	N
47	Yamamoto et al. (66)	2013	75	N	N	N	N	NS	Y (discussion)
48	Wendler et al. (67)	2012	6	N	N	Y	N	NS	Y (discussion)
49	Yared et al. (68)	2012	95	N	N	N	N	NS	N
50	Nielsen et al. (69)	2012	525	N	N	Y	N	NS	N
51	Kempfert et al. (70)	2012	51	N	N	N	N	NS	Y (introduction; discussion)
52	Modine et al. (71)	2012	12	N	N	N	N	NS	N
53	Ong et al. (72)	2012	18	N	N	N	N	NS	N
54	Modine et al. (73)	2012	19	N	N	Y	N	NS	Y (discussion)
55	Grube et al. (74)	2011	60	N	N	Y	N	NS	Y (discussion)
56	Lefèvre et al. (75)	2011	130	N	N	Y	N	NS	Y (introduction; discussion)
57	Bruschi et al. (76)	2012	141	N	N	N	N	NS	N
58	Eidet et al. (77)	2015	40	N	N	N	N	NS	N
59	Adams et al. (78)	2014	795	Y	N	N	N	NS	N
60	Grube et al. (79)	2007	86	N	N	N	N	NS	Y (discussion)
61	Hernández-Antolín et al. (19)	2011	76	N	N	Y	N	NS	Y (results; discussion)

62	Fraccaro et al. (80)	2009	3	N	N	Y	N	NS	N
63	Webb et al. (81)	2006	18	N	N	N	N	NS	Y (discussion)
64	Gurvitch et al. (5)	2011	270	N	N	N	N	NS	Y (introduction; discussion)
65	Kempfert et al. (82)	2011	299	Y	N	N	N	NS	Y (discussion)
66	Webb et al. (18)	2007	50	Y	N	N	N	NS	Y (results; discussion)
67	Leon et al. (83)	2010	358	Y	N	N	N	NS	Y (discussion)
68	Kempfert et al. (84)	2011	40	N	N	N	N	NS	Y (introduction; discussion)

N, no; NS, not stated; PMS, patient to maintain skills; Y, yes.

Most of the studies (71 percent) were undertaken in five countries: Germany ($n = 21$; 31 percent), Italy ($n = 10$; 15 percent), U.S.A. ($n = 9$; 13 percent), France ($n = 8$; 12 percent), and Canada ($n = 5$; 7 percent) (Supplementary Table 2).

Of the sixty-eight studies, we only highlight seven (10 percent) randomized controlled trial studies, and thirty-nine (57 percent) comparative studies. The number of included patients in these studies ranged from 3 to 2,069 patients, and 33 (49 percent) of the studies recruited more than 100 patients. Thirty-four (50 percent) studies were single-center studies, and among these, twenty-nine (85 percent) were performed in a public center.

Data Synthesis

Learning curve data extracted from the studies included are presented in detail in Table 1. Moreover, thirty-seven of the included studies (54 percent) mention the learning curve. The learning curve is mentioned in the discussion for thirty-five (95 percent) of these studies; only three studies (8 percent) also mentioned the learning curve in the results section. In the three studies reporting the learning curve in the results section, general characteristics and outcomes are compared between initial patients and subsequent patients for assessing the learning curve (18–20). One study shows that the implantation rate is significantly different between both groups, that is, more favorable in the subsequent patients (19). Another study shows that the rates of procedural success, malposition, and intraprocedural mortality are more favorable, with statistical significance, in the subsequent patient group (18). The final study shows that valve malposition is more frequent in the initial patients; however, no statistical calculations were performed (20). In these three studies, the patient follow-up varies from 6 to 12 months.

Moreover, we observed no trend between the year of publication and the reporting of learning-curve information. In addition, thirty-seven of the studies included (54 percent) do not report funding sources, and no association with the reporting of the learning curve was observed. Finally, sixty articles (88 percent) do not mention a roll-in period. Details of the eight studies mentioning a roll-in period are presented in Table 2.

In addition, it was noted that sixty-five of the studies (96 percent) do not disclose proctorship, whereas authors of twenty-five studies (37 percent) were proctors working with manufacturers of TAVI. Indeed, proctorship was not disclosed in the method section but in the competing interests. Also, we found no mention of the number of patients necessary to maintain skills in any of the studies included. Last, among randomized and controlled studies, three studies were found to mention learning curves (43 percent), and twenty-two studies alluded to learning curves among comparative studies (56 percent).

Discussion

To our knowledge, this study is the first systematic review dealing with the quality of information reported about the learning curve in TAVI procedures.

Most of the articles reviewed mention the learning curve (more than 50 percent), but only very limited reporting and detailing have been found on the learning curve itself (such as roll-in period, proctorship, and maintenance of skills). In spite of this, learning issues were often mentioned in discussions and were mostly considered to be a source of bias (25;26;30;31;33;37;40;55). Only a few studies provided outcome measures that

Table 2. Details of the studies mentioning a roll-in period

Articles with RIP				
Author	Year of publication	Country where the study was undertaken	Number of patients in RIP	RIP with human or animal
Barbanti et al. (33)	2016	Italy	125	Human
Schofer et al. (39)	2014	Germany	3 in each site	Human, simulated bench model and animal
Kasel et al. (43)	2014	Germany	25	Human
Takagi et al. (20)	2011	Italy	NS	NS
Adams et al. (78)	2014	USA	3 in each site	Human
Kempfert et al. (82)	2011	Germany	150 first patients	Human
Webb et al. (18)	2007	Canada	25 first patients	Human
Leon et al. (83)	2010	U.S.A.	NS	Minimal operator experience with the TAVI procedure was initiated

NS, not stated; RIP, roll-in period.

showed the difference between patients treated in an early phase and those treated later in the study (18–20). In light of these studies, the implantation rate and the valve malposition were outcomes that directly connected to the training of the operators, and this is consistent with previous studies on the topic (85).

In a few studies, the exclusion of a start-up phase is believed to be of paramount importance in providing a more objective evaluation of new devices, without skewing from less-experienced operators (86). Moreover, the experience of the operators is not clearly stated in the studies; however, some authors specify that centers with more TAVI experience trended toward fewer complications than sites with little or no previous experience (24;31;51;57;70). These many allusions to the learning curve remain very heterogeneous in terms of details. As shown by Motte et al. (9), this is probably due to the fact that no guidelines exist for reporting clinical trials on implantable medical devices. However, this same article has determined some relevant items for reporting clinical trials on implantable medical devices, and the learning curve was identified as one of them.

It is remarkable to note that of studies that mention the learning curve, more than three quarters do not discuss a roll-in period. When a roll-in phase was described, it was very disparate between studies. Indeed, a roll-in patient number was not specified in two studies with a roll-in phase (20;83). It was also difficult to know whether training sessions were carried out in humans or animal models in these articles. In addition, some studies described that training would end after a predetermined number of patients, at which point the operator could be considered well-trained. The studies proposed to compare the first patients for whom the technique has been used with the same number of patients after "expertise" is reached (18;82). We remain skeptical about this predetermined roll-in patient number, which seems to have been always arbitrarily determined. Indeed, to our knowledge, although there is no consensus on a reasonable minimum number of patients, studies generally suggest that this number should be between ten and twenty cases (10;87). Consequently, most of the predetermined roll-in patient numbers we found here did not match this range of cases, and it is difficult to understand how the numbers were selected by the study designers.

With very few exceptions, the proctorship was not mentioned in the studies included. This must be linked with the notable percentage of authors who were proctors themselves. Many authors argue that acquisition of expertise in technology and procedures, such as TAVI, must be a gradual process based on an educational experience that should pass through a structured training with different levels of supervision, such as the preceptorship and the proctorship (10;11). This experiential training is important to consider, partly because the number of TAVI programs is proliferating and that it is necessary to plan learning phases in these future programs. It has also been demonstrated that a careful monitoring of the learning curve may have important clinical and economic implications in the development of TAVI procedures (7;85). Although evolving skills can be evaluated during the supervision period, the learning curve goes on after completing any form of training and is a lifelong process. To monitor a center's TAVI outcomes or individuals performing the procedure, some statistical tools can be used. The cumulative summation (CUSUM) test was first introduced to analyze time-series based on industrial processes, and most recently the learning curve-cumulative summation (LC-CUSUM) was designed to determine when a level of expertise has been attained (17;88). This method has been reported to be useful in monitoring a learning curve with regard to the incidence of perioperative complications. Therefore, studies dealing with TAVI procedures should ideally evoke a protocol in which a learning curve would have been anticipated, but we found that in many studies this was not the case (9).

The introduction of new-generation percutaneous aortic valves in clinical practice obliges operators to undergo continuous technical updating and investigate possible limitations of the newly adopted devices (27;71). The expertise of operators could help to improve not just the practices, but also the existing devices. Then, the evolution of the devices must progress toward that of an ease of use and a rapid learning. Furthermore, various transcatheter aortic valves exist on the market, and hospitals can sometimes be forced to change their percutaneous valve preference because of cost considerations. This requires further training with these new devices.

In light of our present work, we propose some criteria that may be helpful when considering the generalizability of results from medical device studies regarding the learning curve. First, the roll-in phase should be systematically reported in the methods section, and the number of patients treated in the roll-in and the duration of this phase should be specified. This could be presented as a protocol associated with the article explaining this in detail. Also, the involvement of a proctor should be reported because it has been proved that expert tutoring provides better results to improve patient outcomes (17). Finally, if no specific training has been necessary because the operators are already well-trained with the technique used in the paper (e.g., when the technique is not new), this should be explained and justified by providing the experience of the operators. It could be helpful to know, for example, the number of cases already treated with the technique by each operator.

The present study has several limitations that should be addressed. First, we did not retrieve full-text versions of all the articles we identified. Although we made every effort to collect the articles, some articles were unobtainable. In addition, we only focused here on articles referenced by PubMed and EMBASE. We did not used additional databases for this systematic review due to resource and time restrictions.

Conclusion

The present systematic review highlights that many prospective studies on TAVI over the past 10 years mention learning curve as a core component of successful TAVI procedures. However, the quality of information about the learning curve reported is relatively poor; only very limited reporting material has been found, whereas some details about roll-in period, proctorship, number of cases to maintain skills should be expected.

Supplementary Material. The supplementary material for this article can be found at https://doi.org/10.1017/S0266462320000100

Conflict of Interest. The authors declare that they have nothing to disclose.

References

1. **Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, et al.** Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med.* 2011;**364**:2187–98.
2. **Vandvik PO, Otto CM, Siemieniuk RA, Bagur R, Guyatt GH, Lytvyn L, et al.** Transcatheter or surgical aortic valve replacement for patients with severe, symptomatic, aortic stenosis at low to intermediate surgical risk: A clinical practice guideline. *Br Med J.* 2016;**354**:i5085.
3. **Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, et al.** 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): A randomised controlled trial. *Lancet (Lond., Engl.)* 2015;**385**:2477–84.
4. **Généreux P, Cohen DJ, Mack M, Rodes-Cabau J, Yadav M, Xu K, et al.** Incidence, predictors, and prognostic impact of late bleeding complications after transcatheter aortic valve replacement. *J Am Coll Cardiol.* 2014;**64**:2605–15.
5. **Gurvitch R, Tay EL, Wijesinghe N, Ye J, Nietlispach F, Wood DA, et al.** Transcatheter aortic valve implantation: Lessons from the learning curve of the first 270 high-risk patients. *Catheter Cardiovasc Interv.* 2011;**78**:977–84.
6. **Alli OO, Booker JD, Lennon RJ, Greason KL, Rihal CS, Holmes DR.** Transcatheter aortic valve implantation: Assessing the learning curve. *JACC Cardiovasc Interv.* 2012;**5**:72–79.
7. **Alli O, Rihal CS, Suri RM, Greason KL, Waksman R, Minha S 'ar, et al.** Learning curves for transfemoral transcatheter aortic valve replacement in the PARTNER-I trial: Technical performance. *Catheter Cardiovasc Interv.* 2016;**87**:154–62.
8. **Webb JG, Altwegg L, Boone RH, Cheung A, Ye J, Lichtenstein S, et al.** Transcatheter aortic valve implantation: Impact on clinical and valve-related outcomes. *Circulation.* 2009;**119**:3009–16.
9. **Motte A-F, Diallo S, van den Brink H, Châteauvieux C, Serrano C, Naud C, et al.** Existing reporting guidelines for clinical trials are not completely relevant for implantable medical devices: A systematic review. *J Clin Epidemiol.* 2017;**91**:111–20.
10. **Gurevich S, John R, Kelly RF, Raveendran G, Helmer G, Yannopoulos D, et al.** Avoiding the learning curve for transcatheter aortic valve replacement. *Cardiol Res Pract.* 2017;**2017**:7524925.
11. **Glauber M, Murzi M, Cerillo AG.** Is proctoring mandatory when starting a TAVI program? *Ann Cardiothorac Surg.* 2012;**1**(2):190–93.
12. **Medical Device and Health Technology Evaluation Committee (CNEDiMTS).** *Recommendation, 21st October 2014, Corevalve, Medtronic.* Saint-Denis: French National Health Authority (HAS); 2014.
13. **Medical Device and Health Technology Evaluation Committee (CNEDiMTS).** *Recommendation, 22nd April 2014, Sapien 3, Edwards.* Saint-Denis: French National Health Authority (HAS); 2014.
14. **Amoore JN.** A structured approach for investigating the causes of medical device adverse events. *J Med Eng.* 2014;**2014**:314138.
15. **Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, et al.** Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med.* 2017;**376**:1321–31.
16. **Raman G, Gaylor JM, Rao M, Chan J, Earley A, Chang LKW, et al.** *Quality of reporting in systematic reviews of implantable medical devices.* Rockville, MD: Agency for Healthcare Research and Quality (US); 2012.
17. **Arai T, Lefèvre T, Hovasse T, Hayashida K, Watanabe Y, O'Connor SA, et al.** Evaluation of the learning curve for transcatheter aortic valve implantation via the transfemoral approach. *Int J Cardiol.* 2016;**203**:491–97.
18. **Webb JG, Pasupati S, Humphries K, Thompson C, Altwegg L, Moss R, et al.** Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. *Circulation.* 2007;**116**:755–63.
19. **Hernández-Antolín R.A., García E., Sandoval S., Almería C., Cuadrado A., Serrano J., et al.** Findings of a mixed transfemoral aortic valve implantation program using Edwards and corevalve devices. *Rev Esp Cardiol.* 2011;**64**:35–42.
20. **Takagi K, Latib A, Al-Lamee R, Mussardo M, Montorfano M, Maisano F, et al.** Predictors of moderate-to-severe paravalvular aortic regurgitation immediately after CoreValve implantation and the impact of postdilatation. *Catheter Cardiovasc Interv.* 2011;**78**:432–43.
21. **Leclercq F, Robert P, Labour J, Lattuca B, Akodad M, Macia J-C, et al.** Prior balloon valvuloplasty versus DIRECT transcatheter aortic valve implantation (DIRECTAVI): Study protocol for a randomized controlled trial. *Trials.* 2017;**18**(1): 303. doi:10.1186/s13063-017-2036-y
22. **Deeb GM, Chetcuti SJ, Reardon MJ, Patel HJ, Grossman PM, Schreiber T, et al.** 1-year results in patients undergoing transcatheter aortic valve replacement with failed surgical bioprostheses. *JACC Cardiovasc Interv.* 2017;**10**:1034–44.
23. **Musa TA, Uddin A, Swoboda PP, Fairbairn TA, Dobson LE, Singh A, et al.** Cardiovascular magnetic resonance evaluation of symptomatic severe aortic stenosis: Association of circumferential myocardial strain and mortality. *J Cardiovasc Magn Reson.* 2017;**19**:1–10.
24. **Greenbaum AB, Babaliaros VC, Chen MY, Stine AM, Rogers T, O'Neill WW, et al.** Transcaval access and closure for transcatheter aortic valve replacement: A prospective investigation. *J Am Coll Cardiol.* 2017;**69**:511–21.
25. **Attizzani GF, Ohno Y, Latib A, Petronio AS, Giannini C, Ettori F, et al.** Acute and long-term (2-years) clinical outcomes of the CoreValve 31 mm in large aortic annuli: A multicenter study. *Int J Cardiol.* 2017;**227**:543–49.
26. **Sinning J-M, Petronio AS, Van Mieghem N, Zucchelli G, Nickenig G, Bekeredjian R, et al.** Relation between clinical best practices and 6-month outcomes after transcatheter aortic valve implantation with CoreValve (from the ADVANCE II study). *Am J Cardiol.* 2017;**119**:84–90.
27. **D'Ancona G, Agma HU, Ince H, El-Achkar G, Dißmann M, Ortak J, et al.** Transcatheter aortic valve implantation with the direct flow medical prosthesis: Impact of native aortic valve calcification degree on outcomes. *Catheter Cardiovasc Interv.* 2017;**89**:135–42.

28. **Conte L, Fabiani I, Pugliese NR, Giannini C, La Carruba S, Angelillis M, et al.** Left ventricular stiffness predicts outcome in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation. *Echocardiography (Mt Kisco, NY)*. 2017;**34**:6–13.
29. **Eidet J, Dahle G, Bugge JF, Bendz B, Rein KA, Aaberge L, et al.** Long-term outcomes after transcatheter aortic valve implantation: The impact of intraoperative tissue Doppler echocardiography. *Interact Cardiovasc Thorac Surg*. 2016;**23**:403–09.
30. **Ahn HC, Nielsen N-E, Baranowski J**. Can predilatation in transcatheter aortic valve implantation be omitted?—A prospective randomized study. *J Cardiothorac Surg*. 2016;**11**:124.
31. **Deeb GM, Reardon MJ, Chetcuti S, Patel HJ, Grossman PM, Yakubov SJ, et al.** 3-year Outcomes in high-risk patients who underwent surgical or transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2016;**67**:2565–74.
32. **Thyregod HGH, Holmberg F, Gerds TA, Ihlemann N, Søndergaard L, Steinbrüchel DA, et al.** Heart team therapeutic decision-making and treatment in severe aortic valve stenosis. *Scand Cardiovasc J*. 2016;**50**:146–53.
33. **Barbanti M, Immè S, Ohno Y, Gulino S, Todaro D, Sgroi C, et al.** Prosthesis choice for transcatheter aortic valve replacement: Improved outcomes with the adoption of a patient-specific transcatheter heart valve selection algorithm. *Int J Cardiol*. 2016;**203**:1009–10.
34. **Ribera A, Slof J, Andrea R, Falces C, Gutiérrez E, Del Valle-Fernández R, et al.** Transfemoral transcatheter aortic valve replacement compared with surgical replacement in patients with severe aortic stenosis and comparable risk: Cost-utility and its determinants. *Int J Cardiol*. 2015;**182**:321–28.
35. **Muneretto C, Bisleri G, Moggi A, Di Bacco L, Tespili M, Repossini A, et al.** Treating the patients in the "grey-zone" with aortic valve disease: A comparison among conventional surgery, sutureless valves and transcatheter aortic valve replacement. *Interact Cardiovasc Thorac Surg*. 2015;**20**:90–95.
36. **Pascual Calleja I, Avanzas P, Munoz Navarro AJ, Lopez Otero D, Del Valle R, Jimenez Navarro MF, et al.** Transcatheter aortic valve implantation in very elderly patients: Immediate results and medium term follow-up. *Eur Heart J*. 2015;**36**:895.
37. **Popma JJ, Adams DH, Reardon MJ, Yakubov SJ, Kleiman NS, Heimansohn D, et al.** Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. *J Am Coll Cardiol*. 2014;**63**:1972–81.
38. **Fanning JP, Wesley AJ, Platts DG, Walters DL, Eeles EM, Seco M, et al.** The silent and apparent neurological injury in transcatheter aortic valve implantation study (SANITY): Concept, design and rationale. *BMC Cardiovasc Disord*. 2014;**14**:45.
39. **Schofer J, Colombo A, Klugmann S, Fajadet J, DeMarco F, Tchétché D, et al.** Prospective multicenter evaluation of the direct flow medical transcatheter aortic valve. *J Am Coll Cardiol*. 2014;**63**:763–68.
40. **Webb J, Gerosa G, Lefèvre T, Leipsic J, Spence M, Thomas M, et al.** Multicenter evaluation of a next-generation balloon-expandable transcatheter aortic valve. *J Am Coll Cardiol*. 2014;**64**:2235–43.
41. **Wendt D, Kahlert P, Pasa S, El-Chilali K, Al-Rashid F, Tsagakis K, et al.** Transapical transcatheter aortic valve for severe aortic regurgitation: Expanding the limits. *JACC Cardiovasc Interv*. 2014;**7**:1159–67.
42. **Barbanti M, Petronio AS, Capodanno D, Ettori F, Colombo A, Bedogni F, et al.** Impact of balloon post-dilation on clinical outcomes after transcatheter aortic valve replacement with the self-expanding CoreValve prosthesis. *JACC Cardiovasc Interv*. 2014;**7**:1014–21.
43. **Kasel AM, Cassese S, Ischinger T, Leber A, Antoni D, Riess G, et al.** A prospective, non-randomized comparison of SAPIEN XT and CoreValve implantation in two sequential cohorts of patients with severe aortic stenosis. *Am J Cardiovasc Dis*. 2014;**4**:87–99.
44. **Sawa Y, Saito S, Kobayashi J, Niinami H, Kuratani T, Maeda K, et al.** First clinical trial of a self-expandable transcatheter heart valve in Japan in patients with symptomatic severe aortic stenosis. *Circ J*. 2014;**78**:1083–90.
45. **Hong S-J, Hong M-K, Ko Y-G, Choi D, Hong G-R, Shim J-K, et al.** Multidisciplinary team approach for identifying potential candidate for transcatheter aortic valve implantation. *Yonsei Med J*. 2014;**55**:1246–52.
46. **Fiorina C, Maffeo D, Curello S, Lipartiti F, Chizzola G, D'Aloia A, et al.** Direct transcatheter aortic valve implantation with self-expandable bioprosthesis: Feasibility and safety. *Cardiovasc Revasc Med*. 2014;**15**:200–03.
47. **Reinöhl J, Gutmann A, Kollum M, Von Zur Mühlen C, Baumbach H, Avlar M, et al.** Transfemoral aortic valve implantation: Bleeding events, related costs and outcomes. *J Thromb Thrombolysis*. 2013;**35**:469–75.
48. **Gotzmann M, Thiessen A, Lindstaedt M, Mügge A, Ewers A.** Left atrial diameter, aortic mean gradient, and hemoglobin for risk stratification in patients undergoing transcatheter aortic valve implantation. *Clin Cardiol*. 2013;**36**:228–34.
49. **Kempfert J, Treede H, Rastan AJ, Schönburg M, Thielmann M, Sorg S, et al.** Transapical aortic valve implantation using a new self-expandable bioprosthesis (ACURATE TA™): 6-month outcomes. *Eur J Cardio-Thorac Surg*. 2013;**43**:52–56; discussion 57.
50. **Treede H, Mohr F-W, Baldus S, Rastan A, Ensminger S, Arnold M, et al.** Transapical transcatheter aortic valve implantation using the JenaValve™ system: Acute and 30-day results of the multicentre CE-mark study. *Eur J Cardio-Thorac Surg*. 2012;**41**:e131–8.
51. **Osnabrugge RLJ, Head SJ, Genders TSS, Van Mieghem NM, De Jaegere PPT, van der Boon RMA, et al.** Costs of transcatheter versus surgical aortic valve replacement in intermediate-risk patients. *Ann Thorac Surg*. 2012;**94**:1954–60.
52. **Jegaden O, Lapeze J, Farhart F, de Gevigney G**. Aortic valve stenosis after previous coronary bypass: Transcatheter valve implantation or aortic valve replacement? *J Cardiothorac Surg*. 2012;**7**:47.
53. **Yamamoto M, Meguro K, Mouillet G, Bergoend E, Monin J-L, Lim P, et al.** Comparison of effectiveness and safety of transcatheter aortic valve implantation in patients aged ≥90 years versus <90 years. *Am J Cardiol*. 2012;**110**:1156–63.
54. **Walther T, Thielmann M, Kempfert J, Schroefel H, Wimmer-Greinecker G, Treede H, et al.** PREVAIL TRANSAPICAL: Multicentre trial of transcatheter aortic valve implantation using the newly designed bioprosthesis (SAPIEN-XT) and delivery system (ASCENDRA-II). *Eur J Cardio-Thorac Surg*. 2012;**42**:278–83; discussion 283.
55. **Walther T, Kasimir M-T, Doss M, Schuler G, Simon P, Schächinger V, et al.** One-year interim follow-up results of the TRAVERCE trial: The initial feasibility study for trans-apical aortic-valve implantation. *Eur J Cardiothorac Surg*. 2011;**39**:532–37.
56. **Modine T, Obadia JF, Choukroun E, Rioufoul G, Sudre A, Laborde JC, et al.** Transcutaneous aortic valve implantation using the axillary/subclavian access: Feasibility and early clinical outcomes. *J Thorac Cardiovasc Surg*. 2011;**141**:487–91, 491.e1.
57. **John D, Buellesfeld L, Yuecel S, Mueller R, Latsios G, Beucher H, et al.** Correlation of device landing zone calcification and acute procedural success in patients undergoing transcatheter aortic valve implantations with the self-expanding CoreValve prosthesis. *JACC Cardiovasc Interv*. 2010;**3**:233–43.
58. **Krane M, Deutsch M-A, Bleiziffer S, Schneider L, Ruge H, Mazzitelli D, et al.** Quality of life among patients undergoing transcatheter aortic valve implantation. *Am Heart J*. 2010;**160**:451–57.
59. **Clavel M-A, Webb JG, Pibarot P, Altwegg L, Dumont E, Thompson C, et al.** Comparison of the hemodynamic performance of percutaneous and surgical bioprostheses for the treatment of severe aortic stenosis. *J Am Coll Cardiol*. 2009;**53**:1883–91.
60. **Grube E, Buellesfeld L, Mueller R, Sauren B, Zickmann B, Nair D, et al.** Progress and current status of percutaneous aortic valve replacement: Results of three device generations of the CoreValve revalving system. *Circ Cardiovasc Interv*. 2008;**1**(3):167–75.
61. **Wöhrle J, Gonska B, Rodewald C, Seeger J, Scharnbeck D, Rottbauer W.** Transfemoral aortic valve implantation with the New Edwards Sapien 3 valve for treatment of severe aortic stenosis-impact of valve size in a single center experience. *PLoS One*. 2016;**11**:e0151247.
62. **Gooley RP, Talman AH, Cameron JD, Lockwood SM, Meredith IT.** Comparison of self-expanding and mechanically expanded transcatheter aortic valve prostheses. *JACC Cardiovasc Interv*. 2015;**8**:962–71.
63. **Kapadia S, Stewart WJ, Anderson WN, Babaliaros V, Feldman T, Cohen DJ, et al.** Outcomes of inoperable symptomatic aortic stenosis patients not undergoing aortic valve replacement: Insight into the impact

of balloon aortic valvuloplasty from the PARTNER trial (Placement of AoRtic TraNscathetER Valve trial). *JACC Cardiovasc Interv*. 2015;**8**:324–33.

64. **Reardon MJ, Adams DH, Coselli JS, Deeb GM, Kleiman NS, Chetcuti S, et al.** Self-expanding transcatheter aortic valve replacement using alternative access sites in symptomatic patients with severe aortic stenosis deemed extreme risk of surgery. *J Thorac Cardiovasc Surg*. 2014;**148**:2869–76.e1–7.
65. **Spethmann S, Dreger H, Baldenhofer G, Pflug E, Sanad W, Stangl V, et al.** Long-term Doppler hemodynamics and effective orifice areas of Edwards SAPIEN and Medtronic CoreValve prostheses after TAVI. *Echocardiography (Mt Kisco, NY)*. 2014;**31**:302–10.
66. **Yamamoto M, Hayashida K, Mouillet G, Chevalier B, Meguro K, Watanabe Y, et al.** Renal function-based contrast dosing predicts acute kidney injury following transcatheter aortic valve implantation. *JACC Cardiovasc Interv*. 2013;**6**:479–86.
67. **Wendler O, Dworakowski R, Monaghan M, MacCarthy PA.**. Direct transapical aortic valve implantation: A modified transcatheter approach avoiding balloon predilatation. *Eur J Cardio-Thorac Surg*. 2012;**42**:734–36.
68. **Yared K, Garcia-Camarero T, Fernandez-Friera L, Llano M, Durst R, Reddy AA, et al.** Impact of aortic regurgitation after transcatheter aortic valve implantation: Results from the REVIVAL trial. *JACC Cardiovasc Imaging*. 2012;**5**:469–77.
69. **Nielsen HHM, Klaaborg KE, Nissen H, Terp K, Mortensen PE, Kjeldsen BJ, et al.** A prospective, randomised trial of transapical transcatheter aortic valve implantation vs. surgical aortic valve replacement in operable elderly patients with aortic stenosis: The STACCATO trial. *EuroIntervention J Eur Collab Work Group Interv Cardiol Eur Soc Cardiol*. 2012;**8**:383–89.
70. **Kempfert J, Van Linden A, Kim W-K, Blumenstein J, Rolf A, Möllmann H, et al.** Ventricular function assessed by MRI after transapical aortic valve implantation: Apical trauma or simple and safe access? *Innov Technol Tech Cardiothorac Vasc Surg*. 2012;**7**:109.
71. **Modine T, Sudre A, Delhaye C, Fayad G, Lemesle G, Collet F, et al.** Transcutaneous aortic valve implantation using the left carotid access: Feasibility and early clinical outcomes. *Ann Thorac Surg*. 2012;**93**:1489–94.
72. **Ong SH, Bauernschmitt R, Schuler G, Mueller R**. Short- and mid-term safety and effectiveness of transcatheter aortic valve implantation in a failing surgical aortic bioprosthesis. *Eur J Cardio-Thorac Surg*. 2012;**42**:268–76; discussion 276.
73. **Modine T, Sudre A, Collet F, Delhaye C, Lemesles G, Fayad G, et al.** Transcutaneous aortic valve implantation using the axillary/subclavian access with patent left internal thoracic artery to left anterior descending artery: Feasibility and early clinical outcomes. *J Thorac Cardiovasc Surg*. 2012;**144**:1416–20.
74. **Grube E, Naber C, Abizaid A, Sousa E, Mendiz O, Lemos P, et al.** Feasibility of transcatheter aortic valve implantation without balloon predilation: A pilot study. *JACC Cardiovasc Interv*. 2011;**4**:751–57.
75. **Lefèvre T, Kappetein AP, Wolner E, Nataf P, Thomas M, Schächinger V, et al.** One year follow-up of the multi-centre European PARTNER transcatheter heart valve study. *Eur Heart J*. 2011;**32**:148–57.
76. **Bruschi G, De Marco F, Oreglia J, Colombo P, Barosi A, Botta L, et al.** Transcatheter aortic valve implantation for severe aortic stenosis after mitral valve surgery. *G Ital Cardiol*. 2012;**13**:170S.
77. **Eidet J, Dahle G, Bugge JF, Bendz B, Rein KA, Fosse E, et al.** Transcatheter aortic valve implantation and intraoperative left ventricular function: A myocardial tissue Doppler imaging study. *J Cardiothorac Vasc Anesth*. 2015;**29**:115–20.
78. **Adams DH, Popma JJ, Reardon MJ**. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;**371**:967–68.
79. **Grube E, Schuler G, Buellesfeld L, Gerckens U, Linke A, Wenaweser P, et al.** Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding CoreValve prosthesis: Device success and 30-day clinical outcome. *J Am Coll Cardiol*. 2007;**50**:69–76.
80. **Fraccaro C, Napodano M, Tarantini G, Gasparetto V, Gerosa G, Bianco R, et al.** Expanding the eligibility for transcatheter aortic valve implantation the trans-subclavian retrograde approach using: The III generation CoreValve revalving system. *JACC Cardiovasc Interv*. 2009;**2**:828–33.
81. **Webb JG, Chandavimol M, Thompson CR, Ricci DR, Carere RG, Munt BI, et al.** Percutaneous aortic valve implantation retrograde from the femoral artery. *Circulation*. 2006;**113**:842–50.
82. **Kempfert J, Rastan A, Holzhey D, Linke A, Schuler G, van Linden A, et al.** Transapical aortic valve implantation: Analysis of risk factors and learning experience in 299 patients. *Circulation*. 2011;**124**:S124–129.
83. **Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, et al.** Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;**363**:1597–607.
84. **Kempfert J, Rastan AJ, Beyersdorf F, Schönburg M, Schuler G, Sorg S, et al.** Trans-apical aortic valve implantation using a new self-expandable bioprosthesis: Initial outcomes. *Eur J Cardio-Thorac Surg*. 2011;**40**:1114–19.
85. **Lunardi M, Pesarini G, Zivelonghi C, Piccoli A, Geremia G, Ariotti S, et al.** Clinical outcomes of transcatheter aortic valve implantation: From learning curve to proficiency. *Open Heart*. 2016;**3**:e000420.
86. **Khawaja MZ, Wang D, Pocock S, Redwood SR, Thomas MR.** The percutaneous coronary intervention prior to transcatheter aortic valve implantation (ACTIVATION) trial: Study protocol for a randomized controlled trial. *Trials*. 2014;**15**:300.
87. **Vallely MP, Wilson MK, Adams M, Ng MKC**. How to set up a successful TAVI program. *Ann Cardiothorac Surg*. 2012;**1**(2):185–89.
88. **Papanna R, Biau DJ, Mann LK, Johnson A, Moise KJ.** Use of the learning curve-cumulative summation test for quantitative and individualized assessment of competency of a surgical procedure in obstetrics and gynecology: Fetoscopic laser ablation as a model. *Am J Obstet Gynecol*. 2011;**204**:218.e1–9.