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Review Article

Development and application of Reverse Systematic Review on laparoscopic radical prostatectomy

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Abstract

Context: Evidence-based medicine was widely used in the context of diverse surgical treatments through several systematic reviews (SR). Despite the high level of evidence from these reviews, the specificity of the analyzed outcomes makes it difficult to establish the state of maturity of the analyzed technique neglecting significant bias. *Objective:* To describe a novel SR methodology based on a temporal population analysis in a Reverse Systematic Review utilizing the case of well-established laparoscopic radical prostatectomy (LRP). *Evidence acquisition:* A systematized search was performed in order to obtain the primary studies feeding SR for the composition of a complete database, covering clinical-surgical and bibliometric variables. Quantitative, qualitative, and temporal correlations of studies variables were performed to determine trends regarding results, geographic distribution and bibliometrics to delineate the development and trends of LRP between 2000 and 2017. *Evidence synthesis:* Among a total of 353 SR found, 40 were included and provided 238 primary studies elected to the database composition. An accumulation of studies was found on the Europe-USA axis predominantly in 4 preeminent scientific journals, which scientifically influenced the profile of publications, mainly until 2011 when interest clearly migrates to robotic-assisted surgery reducing the influence of these centers in the development of LRP in an upfront reversal in the standard of publications with a clear shift between LRP and robotic-assisted surgery studies. Operative time, blood loss, and conversion to open surgery showed trend to reduction and only biochemical recurrence (among *PENTAFECTA)* positively correlated with the year of publication, all with stabilization throughout the period. *Conclusion:* The Reverse Systematic Review proved to be feasible and effective in demonstrating the evolution of a surgical technique, outlining its "Natural History," which is not captured in the standard SR. In addition, it allowed to identify the presence of scientific influencers and potential biases in the composition of the best evidence in the literature, as well as to trace the curves of development until its technical-scientific maturity. Further studies to test the reproducibility of this methodology may aid in the comparison of diverse surgical techniques. *Patient summary:* This temporal study analyzed the variables inherent to the publications and the patients in the primary studies of SRs that approached a specific surgical technique. The results demonstrated the scientific maturity of the technique and the vulnerability to scientific influencers in the history of its development.

Keywords: Prostatectomy; Methodology; Reverse systematic review; Research design

1. Introduction

The evolution of the surgical treatment of prostate cancer resulted in the polarization of the 3 main techniques, generating a spectrum formed by 2 extremes represented by retropubic radical prostatectomy (RRP) and robot-assisted radical prostatectomy (RARP), among them the laparoscopic radical prostatectomy (LRP).

Throughout this history, the comparison between the 3 techniques was a fertile ground for evidence-based medicine (EBM), generating several works of literature reviews, among them the systematic reviews (SR). Considered the best evidence, especially if based on Randomized Clinical Trials

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(RCTs), SRs allow us to gather the best results from the studies in order to answer a specific clinical question [1,2]. However, this specificity limits the extrapolation of the results to other scenarios and excludes other secondary variables that influence the primary outcomes. In addition, the comparative studies between the 3 techniques do not evaluate their maturity, which can generate a bias when comparing a mature and well-established technique with another still in stages of improvement.

Despite the wide variety of methodological review studies, evaluating the stage of scientific development of a surgical technique is challenging, since there is no specific analytical method for this purpose [3]. Given this context, this study primarily seeks, through a broad population analysis, to propose a novel methodology able to delineate the "Natural History" of a surgical technique along its timeline. It is a new systematized review model with the objective of identifying how the various variables related to the technique behaved by analyzing their interrelations in the timeline, allowing possible projections for the future and exposing significant bias neglected by standard SR.

2. Evidence acquisition

2.1. Establishment of the methodology

Conceptually, SRs allow the selection of compatible primary studies in order to answer a specific clinical question. In this way, clinical evidence starts from global knowledge and is filtered until it reaches specific knowledge. Considering that this process inherently eliminates several secondary variables, this new methodology proposes to follow the reverse path, starting from the specific knowledge of the systematic revisions and returning to its primary studies. Table 1 compares the meta-analysis and the proposed novel reverse approach.

2.2. Search strategy

To prove the feasibility of this new methodology, the authors decided to test it with a technique that is well established within the world urological scenario and places between the extremes of a spectrum formed by the RRP and the RARP, the LRP. Thus, systematized research was carried out in search of articles of SRs, with or without meta-analysis that approached the LRP technique, in January 2018. The following databases were used: *PubMed, Web of Science, Cochrane Library, Embase, ProQuest, CINAHL (The Cumulative Index to Nursing and Allied Health Literature), BVS/Bireme*, and *Scopus.* The period in the literature was between January 1, 2000 until December 31, 2017, and the search strategies in each database are related in Supplementary material (Appendix A).

Table 1
Comparison between the characteristics of systematic reviews with meta-analysis and the reverse systematic review.

	Meta-analysis	Reverse systematic review
Question	Specific	Wide
Search criteria	Wide	Wide
Eligibility	Homogeneous	Heterogeneous
Bias search	Initial	Final
Statistical analysis	Meta-analysis	Temporal correlation
Intention	Comparison	Development, influencers, bias

2.3. Inclusion criteria

Two investigators separately reviewed the studies (Moretti TBC, Reis LO) through the title and abstract, electing SRs with or without meta-analysis that included the LRP technique, whether compared to RARP, RRP, or other therapy.

After initial screening, the full texts were analyzed and any discrepancy was resolved after open discussion between the authors. Reviews without a clear and systematized search methodology, integrative methodology, exclusive RARP or RRP reviews, expert consensus, conference summaries, other techniques, and reviews of operative costs were excluded. Due to the difficulty of the databases in standardizing the health descriptors (*MeSH terms*) and classifying a study as a SR, studies were included that, although they did not mention in their methodology that respected *PRISMA* criteria [4], provided a clear description of the systematization of search criteria.

After the selection phase of the reviews, the articles cited in the bibliographic references referring to the LRP were extracted and submitted to a new eligibility process. After exclusion by duplication, the general inclusion criteria were: English language and date of publication between 2000 and 2017. As described above, "Abstracts" or citations in "Report meetings" or "Congress Annals" have been excluded.

2.4. Study eligibility

The selected studies were analyzed integrally by the main author (Moretti TBC) and elected when they presented clinical-surgical variables that were subdivided into 2 groups:

- Perioperative variables: Age (years), BMI (kg/m), initial PSA (ng/dl), initial Gleason score (GS), clinical staging (cT1, cT2, and cT3), lymphadenectomy rate (%), blood loss (ml), blood transfusion rate (%), conversion rate for open surgery (%), bladder catheterization time (days), and length of hospital stay of surgical complications (%).
- Oncologic-functional variables: Pathological GS, pathological staging (pT1, pT2, and pT3) (%), overall margins positivity (%), neurovascular bundle (NVB) preservation (%), global recurrence rate (%), continence rate at 1, 3, 6, 12, and >18 months (%); sexual potency ratio at 1, 3, 6, 12, and>18 months (%).

The largest amount of data available were captured and tabulated in a dedicated spreadsheet (Excel, Microsoft Corporation). To allow for more accurate statistical analysis, studies comparing more than one cohort were dismembered and each cohort was considered as a single study and called a "report" ($n_{(r)}$).

Additionally, in order to provide substrates for the supplementary qualitative analyzes, data referring to the inherent characteristics of the publication itself were gathered in geographical-literary variables and divided into 2 groups:

- Geographical distribution of the studies: Countries of origin of the published works, prioritizing the place where the patients were treated.
- Institutional distribution of studies: Health institutions, hospitals, universities, or research centers responsible for studies.
- Literary distribution of the studies: Scientific journals of publication of the studies.

2.5. Statistical analysis

Descriptive methods (dispersion) and arithmetic were used (estimates of parameters of central tendency, mean, and dispersion, standard deviation, and standard error of the mean).

The relationships among the variables were determined by simple correlation studies, as well as linear and nonlinear regression analysis to verify the function of a better fit between the variables. In order to establish objective criteria, it was decided that the explanatory variable that best represents the temporal evolution of the different relevant variables regarding the evolution of the LRP technique is the year of publication of the referred article.

For the variables with significant simple correlation, a dispersion plot was generated and the regression was calculated with the best fit and representing the distribution without substantially changing the correlation coefficient (r).

In all cases, a significance level of 5% ($P < 0.05$) was used for 2-tailed interpretation. Calculations were performed with the IBM SPSS Statistics v.21 and Curve Expert 1.4 software.

3. Results

We identified 353 review articles in the systematized search. After exclusion of duplications and filters by the inclusion and exclusion criteria, 40 studies were chosen (Appendix B) that cited 605 primary articles on LRP. After exclusion of doubling and eligibility criteria, 238 citations were selected (Appendix C) for data collection for 339 reports and 85,171 patients (Fig. 1).

3.1. Temporal correlation of clinical-surgical variables

3.1.1. Establishment of the explanatory variable: year of publication

The linear regression analysis (r) showed a positive correlation between the year of publication and the duration of the study ($r = 0.403$; $n_{(r)} = 310$; $P < 0.001$) and absence of correlation with the sample size studied ($r = 0.07$; $n_{(r)} = 339$; $P = 0.199$).

Analyzing the duration of the study as a dependent variable, we observed a positive correlation with the sample size ($r = 0.334$; $n_{(r)} = 338$; $P < 0.001$) evidencing a cumulative character of the studies.

3.1.2. Perioperative variables

Among the clinical variables, the simple correlation analysis found was significant with age, BMI, and initial GS. Preoperative PSA and clinical staging (cT1, cT2, cT3, and cT4) showed no significant correlation with the year of publication (Table 2).

In the case of age (Fig. 2A), the regression curve indicated a discrete reduction in the mean age, in years, from 64.84 in 2000 to 61.85 in 2008, increasing to 65.21 in 2016 (SD = 0.15). As for BMI (Fig. 2B), the dispersion data were represented by a linear downward function where mean BMI was discretely reduced from 26.99 kg/m^2 in 2002 to 25.80 kg/m^2 in 2017 (SD = 0.1), without graphical evidence of stabilization. In the case of the initial GS (Fig. 2C), the regression adjustment showed a progressive increase from an average value of 5.76 in 2000 to a maximum stabilization mean value in 2012 of 5.39 (SD = 0.03).

Regarding the surgical variables, a significant negative correlation was found with operative time, blood loss, blood transfusion rate, and conversion rate for open surgery. A significant positive correlation was found with bladder catheterization time, lymphadenectomy rate, and bilateral NVB preservation rate. Variables such as hospitalization time, unilateral NVB preservation rate, nonpreservation rate of NVB, and global complication rate did not present significant correlation over time (Table 2).

In the case of operative time (Fig. 2D), linear regression showed a progressive reduction from 281.66 min in 2000 to a minimum value of 178.76 min in 2017 (SD = 3.71). Regarding the bleeding rate (Fig. 2E), there was a reduction of bleeding from 612.11 ml in 2000 to a minimum of 324.9 ml in 2012, and a subsequent increase to 371.95 ml in 2017 (SD = 13.63). Analyzing the conversion rate for open surgery (Fig. 2F), the adjustment showed a reduction of 2.26% in 2000 to a minimum value of 0.46% in 2013 (SD = 0.15). Regarding the bladder catheterization time (Fig. 2G) a progressive increase of a minimum value in 2002 was found from 7.33 days to 10.44 days in 2016 (SD = 0.22). For lymphadenectomy rate (Fig. 2H), linear regression resulted in a progressive increase over time from 29.43% in 2000 to 66.90% in 2016. Finally, the bilateral preservation rate of the vascular-nervous bundle (Fig. 2I) increased from 2.14% in 2000 to 54.52% in 2011, when it started to decline to 38.11% by 2017 (SD = 2.12).

3.1.3. Oncological-functional variables

Among the oncological variables, a significant positive correlation was found with pathological GS, pT3, and biochemical

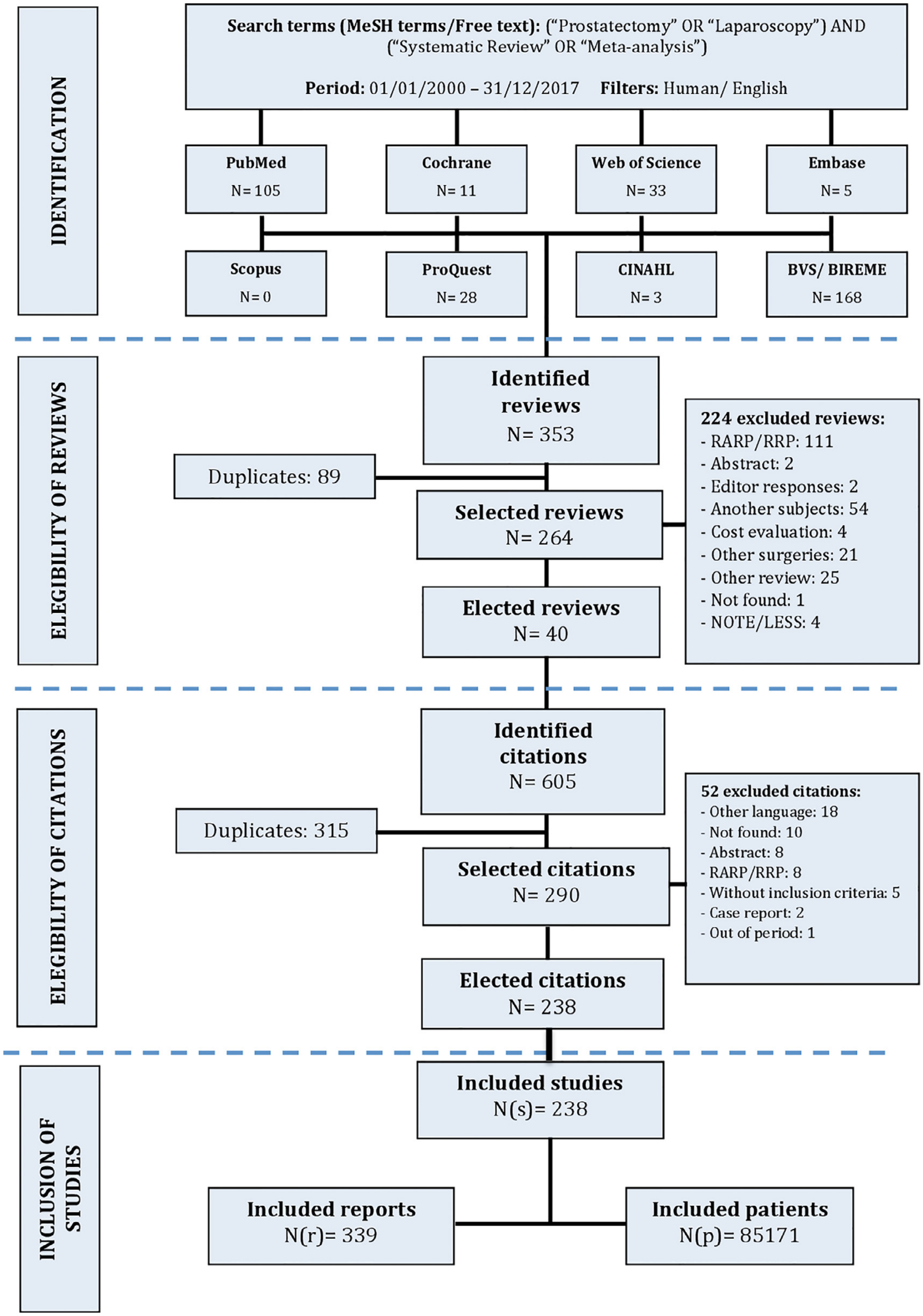


Fig. 1. Study design.

recurrence rate. In the other variables such as pT2, pT4, and all margin positivity rates, no significant correlation was found (Table 2). Regarding the pathological GS (Fig. 3A), mean values progressively increased from 6.21 in 2000 to 6.78 in 2015 (SD = 0.045). In the case of the pT3 rate (Fig. 3B), the correlation indicates a progressive increase from a minimum of 26.02% in 2005 to 34.93% in 2016 (SD = 0.85). Regarding the biochemical recurrence rate (Fig. 3C), the regression curve shows an increase from 3.28% in 2000 to a maximum of 11.70% in 2014 (SD = 0.67).

Table 2
Mean values of the variables and simple correlation with the year of publication.

Perioperative data	Mean	SE	r	P	$n_{(r)}$
Age (y)	62.8	0.2	0.174*	0.002	318
Body mass index − BMI (Kg/m^2)	26.4	0.1	−0.180*	0.027	151
PSA (ng/dl)	8.7	0.2	0.035	0.542	303
Clinical Gleason score	6.2	0.03	0.293*	<0.001	135
Clinical stage − T (%)					
cT1	56.2	1.8	−0.013	0.859	177
cT2	42.6	1.5	0.102	0.177	178
cT3	9.8	1.2	0.089	0.402	90
Operative time (min)	211.9	4.0	−0.378*	<0.001	264
Blood loss (ml)	381.8	14.2	−0.238*	<0.001	215
Conversion to open surgery (%)	1.0	0.2	−0212*	0.008	156
Hospital stay (d)	5.5	0.2	−0.028	0.703	186
Bladder catheterization (d)	8.3	0.2	0.308*	<0.001	181
Lymph node dissection (%)	47.6	2.3	0.346*	<0.001	135
Neurovascular preservation (%)					
Bilateral (%)	44.5	2.2	0.223*	0.006	152
Unilateral (%)	18.8	0.9	0.092	0.289	135
None (%)	43.3	2.2	−0.040	0.618	155
Global complication (%)	16.2	0.8	0.049	0.487	207
Oncologic-functional data	**Mean**	**SE**	r	P	$n_{(r)}$
Pathologic Gleason score	6.4	0.04	0.334*	0.002	80
Pathologic stage (%)					
pT2	70.2	1.0	−0.120	0.065	237
pT3	28.3	0.9	0.195*	0.003	223
pT4	2.8	0.5	−0.046	0.724	62
Positive surgical margins − PSM (%)					
Global	20.3	0.5	−0.005	0.937	281
pT2 PSM	12.4	0.5	−0.026	0.741	166
pT3 PSM	40.9	1.3	0.077	0.355	147
pT4 PSM	87.5	4.3	−0.281	0.102	35
Biochemical recurrence (%)	9.9	0.7	0.249*	0.004	130
Continence rate (%)					
1 mo	38.1	2.8	−0.043	0.738	64
3 mo	62.5	1.8	−0.096	0.277	130
6 mo	77.4	1.3	−0.022	0.822	107
12 mo	85.2	0.9	0.056	0.514	140
>18 mo	86.7	2.1	−0.191	0.239	40
Erectile function recovery rate (%)					
1 mo	14.0	1.8	0.116	0.627	20
3 mo	29.9	2.0	0.165	0.205	61
6 mo	44.1	2.3	0.229	0.068	64
12 mo	54.5	1.8	0.078	0.503	77
>18 mo	51.5	3.5	−0.396	0.030	30

$n_{(r)}$ = number of reports; r = Pearson's coefficient; SE = standard error of the mean.
* Significant correlations ($P < 0.05$).

Among the functional variables, no significant correlation over time was found in the rates of continence and sexual potency at any follow-up time (1, 3, 6, and 12 months; Table 2).

3.2. Geographical and literary results

Considering the division by continents, there is an accumulation of works carried out in Europe ($n_{(r)} = 198$; 58.4%), followed by North America ($n_{(r)} = 77$; 22.7%) and Asia ($n_{(r)} = 52$; 15.3%). In a temporal analysis considering the 3 most important continents in the contribution of publications, there is a proportional evolution between Europe, North America, and Asia until 2012. Afterward, North America reduces its contribution until its complete absence of publications from 2014 to 2017. However, Europe and Asia maintain a proportional oscillation, always with greater European contribution.

Analyzing the 98 research institutions where the work was carried out, it is noted that the 10 most cited (10.2%) in the reviews studied were responsible for publishing 161 reports (47.5%), all of which were located in countries:

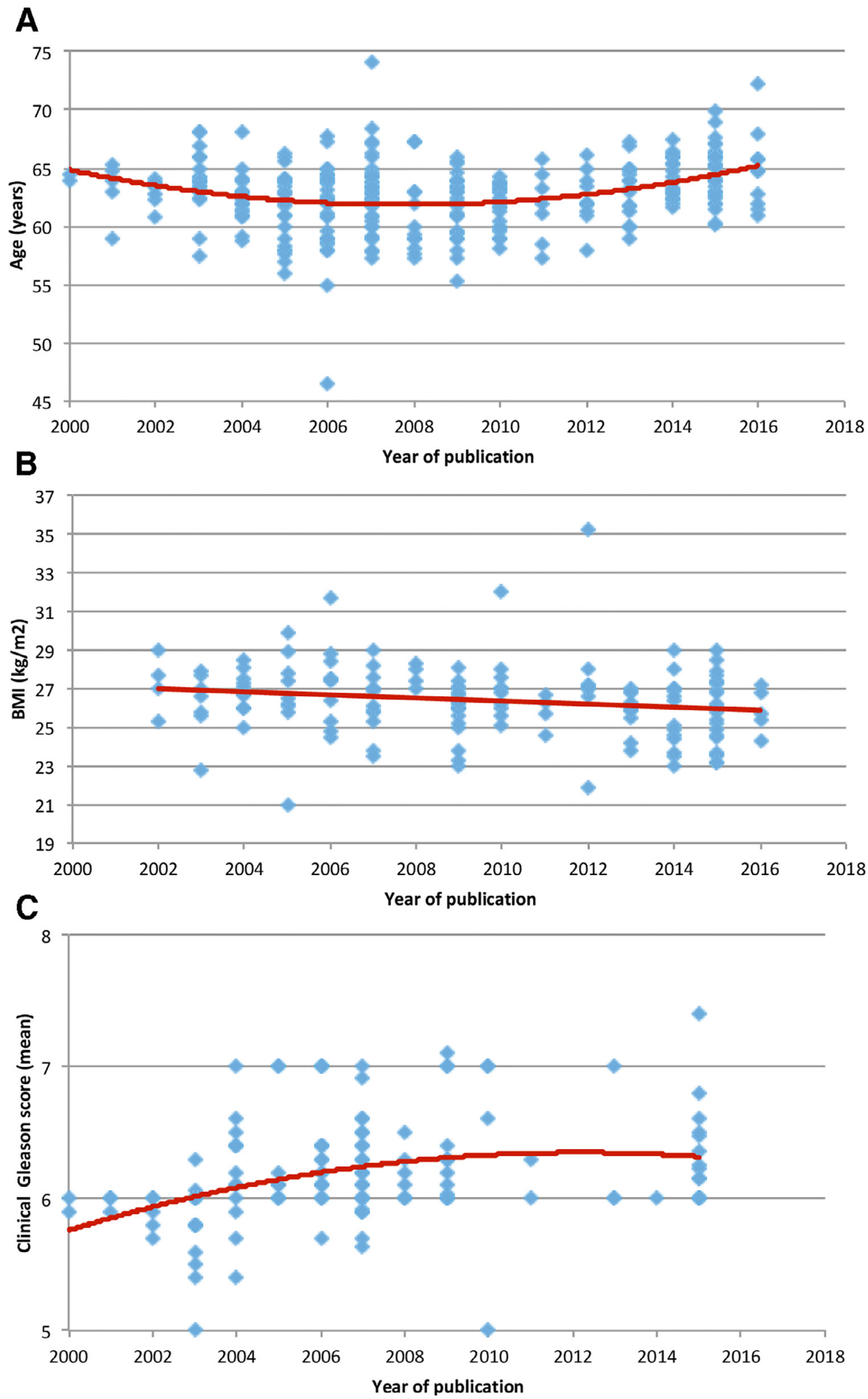
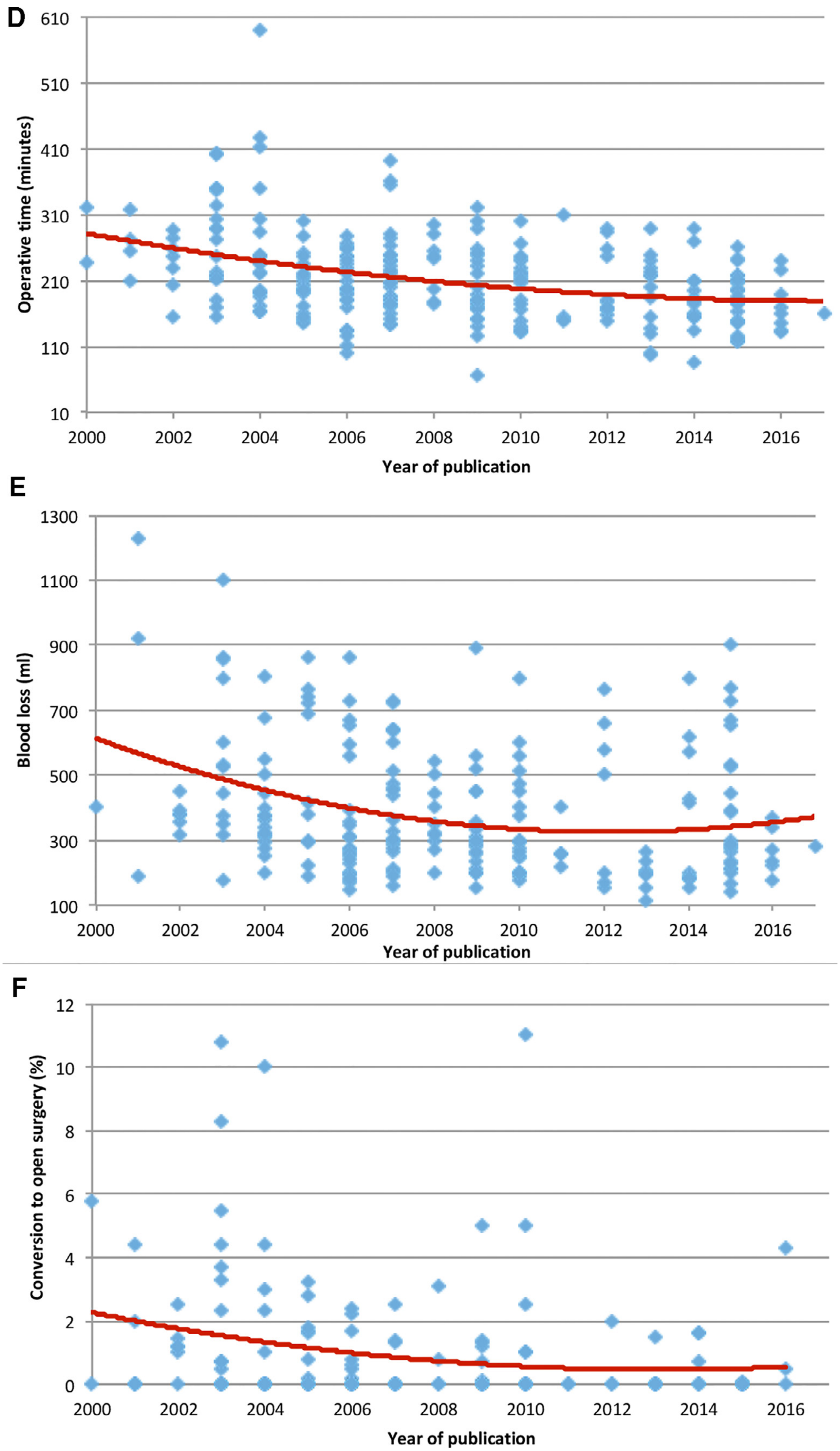


Fig. 2. Scatter plot and regression curves between the year of publication (explanatory variable) and perioperative clinical-surgical variables (response variables): age (years) ($r_{(f)} = 0.334$; SD = 2.739) (A); BMI (kg/m^2) ($r_{(f)} = 0.181$; SD = 1.809) (B); clinical Gleason Score (mean) ($r_{(f)} = 0.334$; SD = 0.386) (C); operative time (min) ($r_{(f)} = 0.387$; SD = 60.268) (D); blood loss (ml)($r_{(f)} = 0.286$; SD = 199.819) (E); conversion to open surgery ($r_{(f)} = 0.232$; SD = 1.924) (F); bladder catheterization ($r_{(f)} = 0.319$; SD = 2.994)(G); lymph node dissection (%)($r = r_{(f)} = 0.346$; SD = 25.47) (H); bilateral neurovascular preservation (%) ($r_{(f)} = 0.339$; SD = 26.13) (I). $r_{(f)}$ = coefficient correlation of regression function; SD = standard deviation of regression function.



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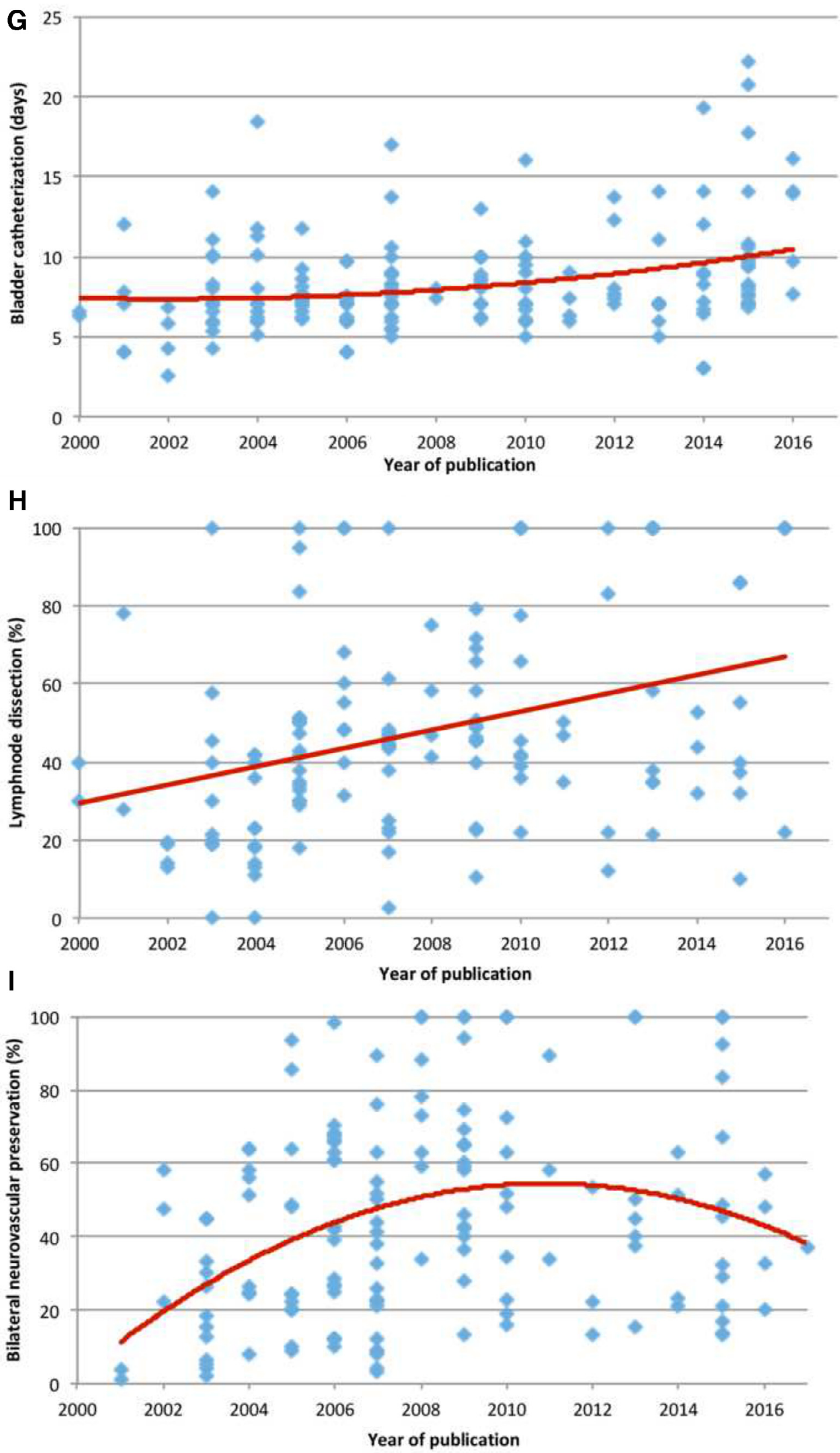

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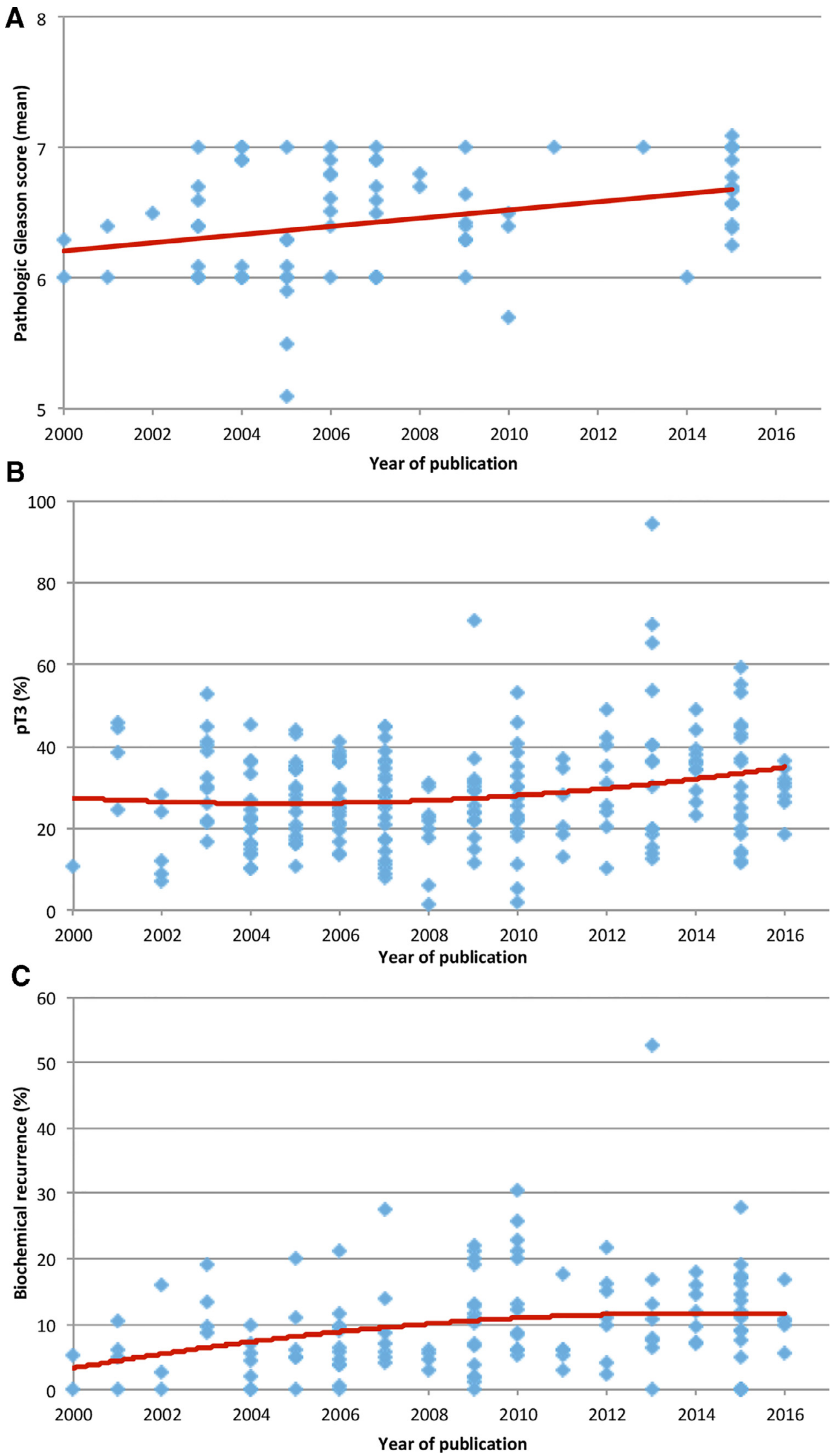

Fig. 3. Scatter plot and regression curves between the year of publication (explanatory variable) and pathologic-functional variables (response variables): pathologic Gleason Score (mean) ($r = r_{(f)} = 0.32$; SD = 0.40) (A); pT3 (%) ($r_{(f)} = 0.213$; SD = 12.62) (B); biochemical recurrence (%) ($r_{(f)} = 0.268$; SD = 7.57) (C). $r_{(f)}$ = coefficient correlation of regression function; SD = standard deviation of regression function.

European countries and the USA. Of these centers, 5 institutions contributed with 33.6% of the reports: *SLK Klinikum Heilbronn* ($n_{(r)} = 35$; 10.3%), *Henri Mondor Hospital* ($n_{(r)} = 26$; 7.7%), *Montsouris Institute* ($n_{(r)} = 20$; 5.9%), *Johns Hopkins University* ($n_{(r)} = 17$; 5.0%) and *Leipzig University* ($n_{(r)} = 16$; 4.7%). Dividing the frequency of publications in a group with the 10 most cited centers and another with the 88 centers we obtained the distribution per year illustrated in Fig. 3B. Throughout the period, there is proportionality, with a predominance of the most cited centers until 2005, where a first inversion occurs until 2007. After, it follows from the equivalence of the groups from 2008 to 2011, where another period of inversion occurs.

Ten scientific journals (22.7%) were used to publish 269 reports (79.4%) over 18 years. Among them, 4 stood out, being responsible for 53.7% of publications: *J Urol* ($n_{(r)} = 51$; 15%), *BJUI* ($n_{(r)} = 46$; 13.6%), *Urology* ($n_{(r)} = 46$; 13.6%) and *Eur Urol* ($n_{(r)} = 39$; 11.5%). In a temporal analysis, the previous data were separated into 2 groups: the first 4 most cited journals and the remaining 40 others. Over the course of 18 years, there is a proportional variation between the 2 groups until 2011. After this date, there is a reversal in the pattern, withdrawing from the scenario the most cited journals and increasing the participation of other journals (Appendix D).

4. Discussion

The history of surgical treatment of prostate cancer was established in 1980 when RRP was described and remained the main treatment for 17 years [5]. In 1992 the laparoscopic technique appeared, but only in 2000 it was improved and reproduced [6−8]. The LRP was much questioned during its implementation since its long-learning curve and reproducibility limited to centers of great volume [9−12]. In 2000, robotic surgery was performed [13,14], and from 2004 it was standardized [15], initiating a polarization of the urological world with the limits delimited by the RRP and RARP and, among them, the LRP.

The evolution of radical prostatectomy is directly related to technological development and innovation investments by major research centers in developed countries. The incorporation of these new technologies in health depends on the results of clinical studies in diverse settings worldwide. This scientific history is immersed in the modern context of EBM and has resulted in several publications in the medical literature with varying degrees of quality and evidence, often compiled in literature reviews.

The development of review study methodologies was a consequence of the large amount of evidence produced exponentially to prove and justify the application of health technologies. However, such methodologies were based on the improvement of evidence filters and statistical tools to answer specific clinical questions, characteristics inherent to SRs with meta-analysis. According to a study by Grant et al. [3], 14 methodologies of literature review were identified and, considering the hierarchy of scientific evidence, SRs with meta-analysis correspond to the higher level, especially when coming from RCTs [2].

As a result of a reverse process of methodological innovation [16], our study developed a new methodology of SR based on a reverse system (Appendix E), describing the stages of development through the practical application in a well-established surgical technique, LRP. Within this methodological system we incorporate an analytic concept known as scientometrics, which study the process of mapping citations and their implications in the development of science [17]. Within the concepts of systems development [18], we discuss the steps of these new methodologies and their quantitative and qualitative results.

As a SR of the literature, rigid criteria for search and eligibility of studies, as proposed by PRISMA, apply to the Reverse Systematic Review, especially in the first stage where SRs are elected. As the goal is to compose a broad population database, the heterogeneity of the studies does not limit and eligibility; on the contrary, it amplifies the sample and legitimizes it as representative of scientific truth.

After establishing the representative sample of the studies that were selected by the best evidence in 18 years of LRP, an expressive number of duplications in the eligibility of the references of the reviews (52%) was noted, indicating a reverberation of the studies within the general conception of scientific knowledge on the LRP that were summarized in 238 studies referring to 85,171 patients.

In the analytical phase, it is fundamental to validate an explanatory variable of temporal characteristic and the year of publication of the studies showed a significant correlation with the beginning and end of the study, that is, its duration. Afterward, 2 groups of variables allowed for analyzes related to the publication and to the patients.

Within the clinical-surgical variables, 2 patterns of results were found. On one side we have the variables without temporal correlation, that is, they did not present change over time. Among the variables of PENTAFECTA [19], 4 of them did not present correlation: complications, PSM, continence rates, and sexual potency. These findings demonstrate that despite the changing clinical profile of the patients (age and staging) these variables remained stable since they are the priorities for any urologist at any stage of development. The biochemical recurrence presented an increase with stabilization in 2014 with 11.70%, probably an effect of the accumulation of long-term studies evaluating oncological outcomes.

Variables related to the surgical technique indicated cumulative patterns of learning curves such as operative time, intraoperative bleeding and conversion to open surgery, which gradually reduced over time. This improvement of the technique occurred even with increased lymphadenectomy rates and preservation of the NVB, demonstrating the improvement of LRP. The generated graphs illustrate the overlap of the isolated learning curves and their temporal correlation, determining “development curves.”

The technical evolution of the LRP throughout its scientific history is immersed in a scenario that can be measured by the reverse methodology through the temporal analysis of the geographic-literary variables. In this analysis, a pattern of oscillation was found in all the graphs determining trends generated by centers of the Europe-United States axis, allowing drawing a profile of the "scientific influencers" within the international urological scenario. Such influence occurs until 2011 where a breakpoint in the chart indicates the USA exit from the group of scientific influencers that coincides with the reduction of the contribution of leading urology journals. The migration of these centers to robotic surgery and the prioritization of magazines in new technologies explain this phenomenon. Asian groups stand out after this break, demonstrating the reproducibility of LRP in different scenarios, with discrete participation from other continents.

The USA involvement as a scientific influencer becomes more evident when we confront the results of the current study with the findings of Childers et al. [20]. In a survey presented in an editorial letter to JAMA in August 2018, the authors extracted data from a financial platform regarding the acquisition and maintenance costs of the *da Vinci* robotic platform between January 1999 and December 2017. With the implementation of the platform in 2010, there was a progressive increase in its deployment with 4,409 robotic systems installed by 2017, 2,862 (65%) in the USA. Regarding the volume of surgery, there was an increase from 136,000 procedures in 2008 to 877,000 in 2017 and, in the latter year, 644,000 (73%) procedures were performed in the USA. In urology, this increase was 85,000 to 118,000 surgeries in the period from 2010 to 2017. In addition, it describes the proportional increase of the deployment of the robotic platform outside the North American scenario, but always with US dominance in the number of acquisitions and number of surgeries. This finding confirms the US exit from the influential axis after 2010, impacting on the scientific interest worldwide, mainly from the main scientific journals, as demonstrated in our study.

Also corroborating the current results, a simple PubMed search by year in the last 20 years publications (made on September 21, 2018) found 1,841 RARP and 1,730 LRP publications, with a clear shift after 2010 that follows the rising trend of robotic systems installed [20] (Appendix F), illustrating diverse maturities and moments for LRP and RARP with significant implications in an eventual literature based comparison between surgical techniques.

Analyzing together the trends of clinical-surgical and geographic-literary variables it can be inferred that the LRP is in a state of technical and scientific maturity. Within a polarized scenario, the LRP developed as a balanced technique between the established RRP and the promising RRP.

Considering the importance of scientific influencers and their migration to robotic surgery, this results in less interest from the scientific community in researching and disseminating results that update the LRP timeline. Even with the emergence of new centers that are reproducing the technique, the power to influence results is reduced, since magazines of greater impact do not have the same interest of the past.

The consequence of the Reverse Systematic Review was to demonstrate the stability of the population sample obtained even in different scenarios of global scientific-literary influence, allowing the generation of reference values for each variable that can be used for future comparisons. This stability, from the statistical point of view, is proven by the high sample size and reduced standard error of the mean, since incorporating any additional value into a graph will hardly change the overall mean. In addition, the ability to demonstrate the maturity status of this methodology allows LRP to be compared with other more secure techniques, such as RRP and RARP, in future studies.

This study is not free of limitations. The composition of a heterogeneous sample allows the temporal analysis but prevents the defragmentation of variables to analyze specific outcomes, a characteristic of SRs with meta-analysis. The presence of correlations with reduced coefficients of determination limits the statistical strength despite being a common feature in heterogeneous population samples. Further multivariate analyzes may reduce such interference. In addition, even if the isolated samples show asymmetric distributions, they are small enough to contribute a significant weight alone, and the overall size is high enough to minimize or even avoid such bias.

The strength of the novel methodology Reverse Systematic Review is beyond scientometrics, adding to the EBM by temporarily analyzing the variables inherent to the publications and the patients in the primary studies of SRs, outlining a surgical technique "Natural History" and exposing scientific influencers, potential biases, and vulnerabilities in the composition of the best evidence available.

5. Conclusion

The reverse methodology proved to be feasible and useful in demonstrating the development of a surgical technique, outlining its "Natural History," which is not captured by the standard SR. The stability of the population sample, the migration of scientific influencers, technological development, and the strong commercial appeal can determine the decay of a surgical technique in several scenarios. It is expected that this methodology will be reproducible for any surgical technique in order to improve the parallel between diverse techniques in the same development curve period.

Authors' Contributions

Moretti TBC: Data collection, data analysis, manuscript writing.

Magna LA: Data analysis, manuscript editing.

Reis LO: Funding acquisition, project development, data analysis, manuscript writing, supervision.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urolonc.2019.06.004.

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