The discovery of the G-spot and verification of its anatomy and histology paved the way to better understanding. Until 2012, the G-spot was defined as a physiological sexual response phenomenon with no identifiable anatomical correlate. The weakness of this definition is that a physiological response cannot exist without an anatomical basis, so the question motivating the present study was formulated: Are current scientific-clinical data sufficient to resolve the controversy about the anatomical existence of a G-spot? It is important to stipulate that no systematic review of the G-spot has hitherto been published. Manual and electronic searches revealed postmortem and in vivo studies describing the G-spot and findings reported within PRISMA-IPD guidelines. The objective of the present review was to provide evidence-based information related to the G-spot. Articles were quality-assessed using validated instruments. Publications on the G-spot from 1950 to May 2019 were reviewed. Of the 279 full-text articles examined, 30 met the eligibility criteria. The findings indicate that there are reliable scientific-clinical data to support the existence of an anatomical G-spot structure. Transient anterior-distal vaginal wall engorgement is caused by blood entrapment within the G-spot structure. Histological examination effectively ruled out the G-spot as the organ cannot be responsible for female ejaculation since no glandular tissue was identifiable. Finally, the results of this study could assist in developing new therapeutic, surgical interventions to treat secondary G-spot dysfunction. Additionally, this review indicates ample opportunities for further scientific-clinical investigations and has thereby moved the field forward.
G-Spot Anatomy and its Clinical Significance: A Systematic Review

In 2014; Herold, 2015) before the anatomical structure of the G-spot was identified (Ostrzenski, 2012). Commentaries, editorials, and letters to editors about the G-spot were published before there was any scientific documentation of the anatomical G-spot. Throughout the centuries, women have reported anterior vaginal wall engorgement during sexual excitement; it was recorded in an ancient Egyptian papyrus. Ostrzenski (2012) discovered the anatomical structure of the G-spot and described it as a small organ embedded within the anterior-distal vaginal wall. Additionally, Ostrzenski (2014) found that the G-spot contributes significantly to the genesis of vaginal ballooning.

The structural existence of the G-spot was verified by postmortem anatomical studies, MRI investigation in vivo, and G-spot histology (Ostrzenski et al., 2014; Ostrzenski, 2014; Maratos et al., 2016). Thabet (2009) conducted an intraoperative anatomical study, and Hoag et al. (2017) performed a postmortem investigation. However, those studies failed to confirm the existence of an anatomical G-spot structure.

METHODS

In order to answer the present study question, this review was organized to: (1) identify the relevant scientific-clinical literature; (2) assess the methodological quality of articles; (3) evaluate the scientific integrity of the reports; (4) appraise the evidence-based levels of the publications; (5) identify diagnostic tools and therapeutic methods for secondary G-spot dysfunction. The eligibility criteria included articles on the G-spot published in peer review journals. Letters to editors, commentaries, and editorials were excluded. This review adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standard guidelines. The following validated instruments were used to assess the methodological quality of articles: (1) the Single-Case Experimental Design Scale, SCED (Tate et al., 2008); (2) Appraising of the Methodological Quality of Cadaveric Studies, QUACS (Wilke et al., 2015); (3) the Scale of Methodological Quality for Clinical Study of Radiological Examinations, SMQCSR (Arrivé et al., 2000); (4) Scientific integrity evaluation by the U.S. National Institute of Health, NIH (2012). The United States Preventive Services Task Force guidelines (August 1989) were used to grade the evidence-based level. Risk of bias was assessed by the ROBIS tool in three phases: (1) assess relevance; (2) identify concerns; (3) judge the risk of bias (Whiting et al., 2016). The research synthesis was evaluated by summarizing the articles and applying the summaries to general synopses in four stages: (1) question addressed in the study, (2) pertinent study selections, (3) data analysis, (4) interpretation of findings.

Manual and electronic searches were carried out from January 1840 to August 2018 in multiple languages and multiple websites. The Medical Subject Headings were used. The following keywords were applied: the female erogenous zone; Gräfenberg zone; Gräfenberg spot; G-spot; G-spot anatomy; G-spot histology; G-spot MRI, G-spotplasty; G-spot amplification; G-spot augmentation; G-shot; G-spot dysfunction.

RESULTS

Thirty of the 279 articles met the eligibility criteria (1.075%): one anatomycase report (3%); nine consecutive anatomical case series studies (30%); six consecutive in vivo MRI case series studies (20%); five histological case series studies (16%); four consecutive ultrasonographic case series studies (13%); four G-spot deficiency and therapy studies (13%); and one randomized study (3%). The number of well-designed and well-executed research studies was low. Methodological quality assessments of the reviewed articles are presented in Table 1.

Gross Anatomy of the G-Spot

The G-spot is described as a tiny structure located within the anterior-distal vaginal wall and lying within its own sac (Ostrzenski, 2012; Ostrzenski et al., 2014; Ostrzenski, 2014). Its anatomical structure can

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*Preventive Services Task Force (USPSTF) put forth the following grading system: Level I: Evidence obtained from at least one properly designed randomized controlled trial. Level II-1: Evidence obtained from well-designed controlled trials without randomization. Level II-2: Evidence obtained from well-designed cohort studies or case-control studies, preferably from more than one center or research group. Level II-3: Evidence obtained from multiple time series designs with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence. Level III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.
entrap blood, which probably accounts for anterior-distal vaginal wall engorgement (Ostrzenski, 2014). Skene’s female urethral glands (Skene, 1880) were previously mistaken for G-spot structures (Thabet, 2009). Hoag et al. (2017) conducted a postmortem study and failed to identify the G-spot anatomical structure; however, this group used a very unorthodox dissection method, which involved amputating the lower extremities, removing the sacrum and pelvic muscles, cystectomy, hysterectomy, and posterior vaginal wall resection. The experimental part of their study was conducted on the extirpated vagina with a partially resected posterior vaginal wall. Such a method has never been described in the literature. It made interpretation difficult because the G-spot structure could have changed in size when it was removed from its surroundings. The original dissection method used to identify the G-spot anatomical structure was performed on an intact vagina in its normal location (Ostrzenski, 2012; Ostrzenski et al., 2014, Ostrzenski, 2014).

Hoag et al. (2017) also applied uneven traction with instruments to the different segments of the extirpated vagina causing the G-spot to change appearance (Fig. 1: the original photograph from Hoag et al., 2017). Consequently, these authors overlooked the G-spot anatomical structure that was visible in their own published Figure 1. The same group overlooked data in the existing literature such as the histological description of a nerve ganglion, which was considered the histological landmark distinguishing the G-spot from the vaginal and urethral walls (Ostrzenski et al., 2014). Additionally, they omitted information from the in vivo MRI study that revealed the G-spot anatomical structure in 100% of cases when vaginal contrast was used (Maratos et al., 2016).

Song et al. (2009) stated that the anterior-distal vaginal wall has intense innervation, which they suggested "could be called the G-spot." However, other researchers disagreed: "Innervation and vasculature were quantitatively the same along the anterior vagina" (Mazloomdoost et al., 2017; Pauls, 2006).

Vaginal nerve fibers produce different transmitters, which could act differently on different structures such as capillaries, the vaginal adventitia, and large blood vessels, controlling blood flow as well as capillary permeability (Pauls, 2005). The neuron distributions within the vaginal wall were reported to have very little practical or scientific-clinical significance (Hoyle, 1996).

Ingelman-Sundberg (1997) revealed intraoperatively that two ligaments located in the anterior-distal vagina were responsible for moving the clitoris downward in the direction of the vagina. These ligaments connected the lateral-anterior-distal vaginal wall to the urethral meatus and continued running to the clitoral body.

**G-spot Histology**

The G-spot was identified histologically as a neurovascular complex containing a nerve ganglion. It was embedded within a fibro-adipose tissue bed with numerous peripheral nerve fibers and bundles. The ganglion distinguished the G-spot from the anterior-distal vaginal and urethral walls. No neuro-ganglion was identified within the anterior-distal vaginal wall by Lee (1841); therefore, the present study was the first to define the characteristic microscopic features of the G-spot.

The vascular composition of the G-spot was described as follows: "The vascular component consists of a large tangled vein-like vasculature structure, with some thrombosed and some collapsed vessels with empty lumens, resembling arteriovenous malformations. There are a few smaller feeding arteries in the adjacent adipose tissue" (Ostrzenski et al., 2014). This review also established the absence of identifiable glandular or erectile tissue within the G-spot structure (Ostrzenski et al., 2014). In the past, it was proposed that anterior vaginal wall ballooning (tenting or engorging) depends upon erectile tissue within the G-spot. The histology ruled out the presence of erectile tissue in the G-spot; vaginal ballooning results from blood entrapment within it (Ostrzenski, 2014).

Immunohistochemical investigations using the ICC marker revealed significantly more circular than longitudinal muscles in the upper part of the posterior vaginal wall as the ICC marker concentration was higher in the posterior vaginal wall (Shafik, 2007). This finding did not correspond to the natural anterior-distal vaginal location of the G-spot (Ostrzenski, 2012; Ostrzenski et al., 2014; Ostrzenski, 2014). The electrovaginogram demonstrated that electrical waves can be interpreted as: "The vaginal electric pacemaker seems to represent the G-spot." Rising pressure within the vaginal wall increased the variable electrical waves. When the vaginal wall was anesthetized, electrical waves were recorded proximally but not distally (Shafik, 2004).

**Female Ejaculation**

De Graaf (1668) described female ejaculation and linked it to the stimulation of an erogenous zone (Jocelyn and Setchell, 1972). Female ejaculation was estimated to occur in between 10% and 54%. Penetrative urethral urine leaks were suggested as the mechanism, and detrusor muscle overactivity was supposedly responsible for this (Pastor, 2013). However, another study documented that the voiding pattern was within expected norms in women experiencing ejaculation (Cartwright et al., 2007).

The absence of secretory gland tissue within the G-spot structure effectively ruled out a role for the G-spot in female ejaculation (Ostrzenski et al., 2014).

**Female Prostate Gland?**

The term "female prostatic gland" was used for the G-spot, but the histology of the G-spot was not consistent with this description since there is no secretory gland tissue (Ostrzenski et al., 2014). Its
Fig. 1. G-spot identification. (a) Within the white circle, close to the right side, there is a structure resembling a half donut, which is directly connected to the lateral vaginal wall veins, and then traverses out of the white circle and fuses with the vaginal wall. The "Putative G-spot" depicted in Figure 1A does not reflect the true G-spot location. (b) The vaginal vestibule bulb does not embrace the distal urethra as illustrated in the original figure. Used with the permission from the J Sex Med Editorial Office. [Color figure can be viewed at wileyonlinelibrary.com]

microscopic characteristics effectively ruled out any comparison between the G-spot and the prostate gland (Ostrzenski et al., 2014).

**PET Scan**

A woman with a severed spinal cord was compared to a healthy woman. Both were subjected to vaginal and/or cervical stimulation and their brain activities were recorded on a PET scan, which revealed that they both reached vaginal orgasms (Whipple and Komisaruk, 2002).

**MRI of the G-Spot**

The in-vivo MRI investigation confirmed the PET scan findings and established that the vagus nerve provided a spinal cord bypass to generate vaginal
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| Goldstein and Berman | Review           | - Diagnostic studies assessing the hemodynamic integrity of the ilio-hypogastric-pudendal arterial bed | - Pharmacologic treatment for atherosclerosis  
- Target therapy to enhance vaginal/clitoral blood flow for nonatherosclerotic conditions | - Atherosclerotic impairment  
- Nonatherosclerotic impairments (vascular disease of the ilio-hypogastric-pudendal arterial bed resulted from pelvic fractures or blunt perineal trauma)  
- G-spot (the arousal phase) dysfunction symptoms:  
  - delayed vaginal engorgement,  
  - diminished vaginal lubrication,  
  - dyspareunia,  
  - diminished vaginal sensation,  
  - diminished vaginal orgasm,  
  - diminished clitoral sensation,  
  - diminished clitoral orgasm  
- The effectiveness and safety for the treatment of female sexual arousal dysfunction.  
- The results demonstrated that the topical Alprostadil applied prior to vaginal intercourse significantly improved the sexual arousal phase of the female subjects associated with sexual arousal deficiency (the G-spot dysfunction)  
- The G-spot anatomical structure existence is a controversial topic and is debated theme  
- Standard questionnaires: Fragebogen zur Lebenszufriedenheit (FLZ) and Kurzfragebogen für sexuelle Probleme (KFSP-F) documented no improvement of sexual fulfillment  
|                    |                  |                                                                             | Alprostadil topical cream (E3 prostaglandin) applied to the clitoris and the G-spot in the vagina prior to vaginal sexual intercourse |                                                                                                                                                                                                                                                                 |
| Liao et al.        | Multicenter randomized study | The Female Sexual Function Index (FSFI), Global Assessment Questionnaire, other FSEP question responses, and post-treatment changes in Female Sexual Distress Scale | A filler injected into the septum between the bladder and the anterior distal vaginal wall  
Autologous adipose tissue transfer |                                                                                                                                                                                                                                                                 |
| Bachelet et al.    | Review           | Not elaborated                                                             | A filler injected into the septum between the bladder and the anterior distal vaginal wall  
Autologous adipose tissue transfer |                                                                                                                                                                                                                                                                 |
| Herold et al.      | Case report      | Decrease vaginal sexual sensation                                            | Surgical intervention on the anterior, distal vaginal wall              |                                                                                                                                                                                                                                                                 |
| Ostrzenski         | Case series study | Preoperatively and postoperatively, a validated and self-completion instrument of Sexual Relationships and Activities Questionnaire (SRA-Q) | Surgical intervention on the anterior, distal vaginal wall              |                                                                                                                                                                                                                                                                 |
orgasms (Komisaruk and Whipple, 2005). Multiplanar high-resolution dynamic MRI technology is useful for evaluating the anatomy of living and postmortem subjects (Maratos et al., 2016; Maravilla et al., 2003; Maravilla et al., 2005; Maravilla and Yang, 2008). The in vivo MRI study by Maratos et al. (2016) documented the presence of the G-spot structure in 100% when vaginal contrast was used and in 62% without it. This group also confirmed Ostrzenski’s findings that the G-spot is located in the anterior-distal vaginal wall and could be identified on either the right or the left side of the urethral wall, but never bilaterally (Ostrzenski et al., 2014; Ostrzenski, 2014).

Ultrasound of the G-spot

Gravina et al. (2008) suggested that ultrasonographic measurement of the urethrovaginal space thickness reveals the location and diameter of the G-spot structure. This space was naturally occupied by the female Skene’s urethral glands and ducts (Skene, 1880; Nettner, 1989). The G-spot was not located in it but within the anterior-distal vaginal wall (Ostrzenski, 2012; Ostrzenski, 2014; Ostrzenski et al., 2014; Maratos et al., 2016).

Genetics of the G-spot

Burri et al. (2010) determined a 56% G-spot prevalence among female twins. The authors offered an explanation for their findings and stated that lack of knowledge about the location of the G-spot and its potential function led to incorrect answers. Genetic Affymetrix probes were studied, and their success in identifying the G-spot location revealed that a G-spot probe with the 5′ end was the most sensitive (Upton et al., 2008).

Therapies for the G-spot

Ostrzenski (2018) established clinical diagnostic criteria for secondary G-spot dysfunction including: (1) secondary inability to reach vaginal orgasm, (2) diminished vaginal engorgement, (3) decreased sensation of the anterior-distal vaginal wall during sexual stimulation, (4) history of traumatic vaginal delivery or anterior-distal vaginal wall surgery, (5) prior conservative medical therapy failure. Vaginal engorgement dysfunction (secondary G-spot dysfunction) could have an atherosclerotic or nonatherosclerotic vasculogenic origin (Goldstein & Berman, 1989). Empirical therapies have been offered for this medical entity, one treatment mode being G-spot amplification by collagen injection. Embolism is the primary clinical concern with this method (Bachelet et al., 2014; Ostrzenski, 2014). Autologous fat transfer by injecting adipose tissue was another suggested therapy for G-spot deficiency; however, an additional study failed to support its validity (Herold et al., 2015). The risk of potential embolization by this therapy was also a concern (Ostrzenski, 2014).

A randomized study demonstrated the safety and effectiveness of topical E1 prostaglandin vaginal cream (Alprostadil) for female sexual arousal dysfunction (Liao, 2008). All therapeutic methods are summarized in Table 2. A form of surgical intervention, G-spotplasty, was recently developed. It can improve female sexual function and help in reaching vaginal orgasms, and restoring vaginal wall engorgement (Ostrzenski, 2018).

DISCUSSION

The “G-spot” is a misleading term as it is not a spot but a tiny anatomical structure within the anterior-distal vaginal wall (Gräfenberg, 1950; Ostrzenski, 2012; Ostrzenski et al., 2014; Ostrzenski, 2014; Maratos et al., 2016). De Graaf (1668) introduced the term “an erogenous zone,” and Gräfenberg (1950) also used it. Addiego et al. (1981) changed the phrase “e:rogenous zone” to “the Gräfenberg zone.” Perry and Whipple (1981) introduced the term “The Gräfenberg spot” and Ladas et al. (1982) used the abbreviated form “G-spot” in their nonacademic book; the media around the globe popularized it.

This review provides information that the G-spot is a separate anatomical structure within the anterior-distal vaginal wall (Ostrzenski, 2012; Ostrzenski et al., 2014; Ostrzenski, 2014; Maratos et al., 2016). It also reveals that anterior-distal vaginal wall engorgement results from blood entrapment within the G-spot structure (Ostrzenski, 2014), and this mechanism is not related to erectile tissue. Clinical diagnostic criteria for secondary G-spot dysfunction were established by Ostrzenski (2018): (1) secondary inability to reach vaginal orgasm, (2) diminished anterior vaginal wall engorgement, (3) decreased sensation of the anterior-distal vaginal wall during sexual stimulation, (4) history of traumatic vaginal delivery or anterior-distal vaginal wall surgery, (5) unsuccessful prior conservative medical therapy. A new surgical procedure, G-spotplasty, offers treatment for secondary G-spot dysfunction (Ostrzenski, 2018). There is room for more clinical-scientific research to distinguish different forms of G-spot deficiency, to examine the role of the G-spot in sexual arousal phase dysfunction, and to investigate how the G-spot affects the rest of the female sexual response cycle. Such clinical-scientific research could establish specific diagnostic tool(s) for the diagnosis of G-spot dysfunction(s) and assist in developing targeted medical and surgical therapies.

The strengths of this review are the in-depth electronic database and manual searches used to select articles, the strict eligibility criteria, data extraction to define outcomes, assessment of the risk of bias, and data synthesis. Validated instruments were used to appraise the scientific-clinical quality of the articles to minimize bias and offer standardized evaluation (Tate et al., 2008; Wilke et al., 2015; Arrivé et al., 2000). NIH criteria (2012) were used to ascertain the scientific integrity of the reports. The United States Preventive Services Task Force guidelines (2012) were deployed to determine the evidence-based level (Table 1). To the best of the author’s knowledge, no previous systematic review study of the G-spot is
available in the medical literature. Finally, to keep the scope of this review manageable, the author focused on clinical-scientific research reports and excluded editorials, communications, and letters to editors.

The primary limitation of the review is the low quality and quantity of published articles on the G-spot. The relatively small number of studies that report specific data about the G-spot precludes meta-analysis. The pool of the available studies is highly variable in terms of study design, population sample, and outcomes. Observational studies inherently harbor biases, and the available literature on the G-spot includes only one report of Level I; all the remaining articles are observational. Lack of a comparison group made it impossible to perform statistical analyses and to draw general conclusions.

This systematic review suggests that further in vivo multiplanar-high resolution-dynamic MRI and ultrasonographic studies are needed. Also, clinical aspects of the G-spot should be explored with particular attention to the diagnosis and therapy of dysfunctions of this structure.

CONCLUSION

Scientific-clinical data support the existence of a G-spot anatomical structure. The histology rules out the presence of erectile or glandular tissue and establishes a nerve ganglion as the G-spot landmark. Female ejaculation is not associated with the G-spot. Blood entrapment within the G-spot structure accounts for vaginal wall enlargement. It also indicates ample opportunities for clinical-scientific research on the G-spot.

REFERENCES
