surgeries

MDPI

Review

A Narrative Review of the Best Anesthesia Care for Endovascular Thrombectomy: Early Diagnosis of the Ischemic Stroke and Evaluation of Risk Factors in Female Population

Filadelfo Coniglione [1,2], Francesco Giuseppe Martire [3,*], Rudin Domi [4], Claudia d'Abate [3], Giulia Donadel [1], Gentian Huti [5], Asead Abdyli [5], Krenar Lilaj [4] and Emilio Piccione [2,6]

1 Department of Clinical Sciences and Translation Medicine, Section of Anesthesiology and Intensive Care, University of Rome "Tor Vergata", 00175 Rome, Italy; filadelfo.coniglione@uniroma2.it (F.C.); donadel@uniroma2.it (G.D.)
2 Department of Surgical Sciences, Catholic University "Our Lady of Good Counsel", 1031 Tirana, Albania; piccione@med.uniroma2.it
3 Department of Molecular and Developmental Medicine, Obstetrics and Gynecological Clinic, University of Siena, 53100 Siena, Italy; claudiadbate94@gmail.com
4 Department of Surgery, University of Medicine, 1031 Tirana, Albania; rdomi73@yahoo.it (R.D.); krenar20@yahoo.com (K.L.)
5 American Hospital, 1031 Tirana, Albania; gentianhuti@yahoo.com (G.H.); aseadabdyli@yahoo.com (A.A.)
6 Department of Surgical Sciences, University of Rome "Tor Vergata", 00175 Rome, Italy
* Correspondence: francescogmartire@libero.it; Tel.: +39-3452205489

Abstract: Background: The increasing incidence of cerebrovascular accidents represents an emerging problem. The rise in risk factors such as lifestyle choices—smoking, poor nutrition, and metabolic diseases—poses a significant challenge for the global healthcare system. The female population, due to physiological conditions and iatrogenic risks, may be at a greater risk of developing ischemic accidents. In addition to these acquired conditions, life phases such as pregnancy or puerperium, and medical conditions like surgical treatments and hormone therapy, may elevate this risk. Methods: This narrative aims to assess the various risk factors specific to the female population and evaluate the appropriate management strategies, including anesthetic support. Anesthesia plays a crucial role in enabling pharmacological procedures, such as thrombolysis, or surgical procedures like thrombectomy, in the management of ischemic cerebrovascular events. Results: The review emphasizes the importance of early recognition of risk factors to ensure prompt diagnosis and the most appropriate treatment options for ischemic events. Anesthesia support has become essential for carrying out necessary medical interventions effectively. Choosing the right anesthesia technique for endovascular thrombectomy is particularly significant, requiring consideration of the patient's characteristics, the timing of diagnosis, and the preferences of the interventional neuroradiologists. Conclusions: It is vital to identify risk factors in the female population early to facilitate timely diagnosis and optimize treatment outcomes. Anesthetic support plays a key role in ensuring that critical procedures, such as thrombolysis and thrombectomy, are carried out effectively. Tailoring anesthesia choices to the patient's individual needs is critical for a successful intervention.

Keywords: anesthesia; gynecology; ischemic stroke; obstetrics; thrombectomy

Citation: Coniglione, F.; Martire, F.G.; Domi, R.; d'Abate, C.; Donadel, G.; Huti, G.; Abdyli, A.; Lilaj, K.; Piccione, E. A Narrative Review of the Best Anesthesia Care for Endovascular Thrombectomy: Early Diagnosis of the Ischemic Stroke and Evaluation of Risk Factors in Female Population. *Surgeries* **2024**, *5*, 1056–1071. https://doi.org/10.3390/surgeries5040085

Academic Editor: Enrico Camporesi

Received: 27 October 2024
Revised: 21 November 2024
Accepted: 26 November 2024
Published: 28 November 2024

1. Introduction

The increasing incidence of cerebrovascular accidents, particularly ischemic strokes, presents substantial medical and financial challenges for healthcare systems worldwide. Recent reports have underscored that ischemic stroke is a major contributor to global morbidity and mortality, placing a considerable burden on patients, families, and healthcare providers [1].

Ischemic stroke occurs when a large cerebral artery becomes occluded by a thrombus or atherosclerotic plaque, leading to a significant reduction in regional blood flow and subsequent cerebral edema. This is particularly devastating when the ischemic insult involves the middle cerebral artery, which is a common site of occlusion and can result in extensive neurological damage [2]. The pathophysiology of ischemic stroke underscores the importance of rapid and effective intervention to minimize brain injury and improve patient outcomes.

Once a clear diagnosis of ischemic stroke is established, the treatment approach is largely determined by the timing of the patient's presentation. For patients who arrive at the emergency department and are diagnosed within 4.5 h of symptom onset, thrombolysis with various thrombolytic agents remains a viable treatment option, aiming to dissolve the clot and restore blood flow [3,4]. However, the efficacy of thrombolysis diminishes significantly after this window, necessitating alternative strategies [5].

In cases where the thrombolytic window has elapsed, mechanical thrombectomy emerges as the preferred intervention, particularly when initiated within the first 6 h of symptom onset. Mechanical thrombectomy involves the physical removal of the thrombus from the occluded vessel, which can be lifesaving and significantly improve functional outcomes in patients with large vessel occlusions. This procedure has revolutionized stroke care, offering hope to patients who would otherwise face severe disability or death.

The evolution of stroke management, including the use of advanced imaging techniques and the refinement of endovascular procedures, has dramatically changed the landscape of acute ischemic stroke treatment. As research continues to advance, the focus remains on optimizing treatment strategies, including the critical decision-making process surrounding the use of thrombolysis and mechanical thrombectomy, to ensure that patients receive the most effective care possible in the critical moments following a stroke.

The first aim of this narrative review is to provide all the most adequate information to allow an early diagnosis of the ischemic accident, especially in the female population, starting from external risk factors such as lifestyle, i.e., smoking, poor nutrition, metabolic diseases [6], physiological risk factors such as pregnancy and puerperium, and iatrogenic risk factors such as surgical procedure and hormonal treatment, and then discussing the anesthetic support actions to thrombolysis and thrombectomy procedures. Currently, there is no universal agreement on the ideal anesthetic agent or approach, and the existing literature often presents conflicting viewpoints on numerous critical aspects. Factors such as patient variability, differing procedural requirements, and the diverse range of anesthetic options contribute to the lack of a single, universally preferred approach. Consequently, the secondary objective of this narrative review is to examine commonly accepted anesthetic practices and methodologies, analyzing their strengths and limitations in various contexts. Through this exploration, we aim to shed light on whether a superior anesthetic approach may exist, considering both efficacy and safety across patient populations.

2. Materials and Methods

The literature research by the MEDLINE database was performed with the purpose of identifying all English-language papers focusing on anesthesia care for endovascular thrombectomy considering obstetrical and gynecological risk factors. The research considered all papers within the last 20 years, from 2003 to December 2023. Two authors (FC and FGM) from January 2024 to June 2024, combined Medical Subject Headings (MeSH) search terms and the following keywords to screen studies: "Anesthesia", "Gynecology", "Hormonal Treatment", "Ischemic Strokes", "Obstetrics", "Thrombectomy". We considered, for possible inclusion in the narrative review, clinical trials, retrospective studies, case–control studies, and observational prospective studies.

The papers identified within this research were considered eligible if they met the scope of this narrative review, i.e., to highlight the fundamental role of anesthesia care for treatment of ischemic accidents by thrombosis, particularly in patients with an increased risk from obstetrical and gynecological conditions.

3. Results

Two authors (F.G.M. and F.C.) independently conducted the research and subsequently analyzed all the articles and, at the end of evaluation, they included 68 articles in this review (Figure 1). All points of the research topic were discussed, such as risk factors during and after surgical procedure, obstetrical risk conditions, gynecological risk conditions, hormonal therapy risk conditions, modifiable and non-modifiable risk factors (like lifestyle, thrombophilia) and all types of anesthesia support during thrombectomy.

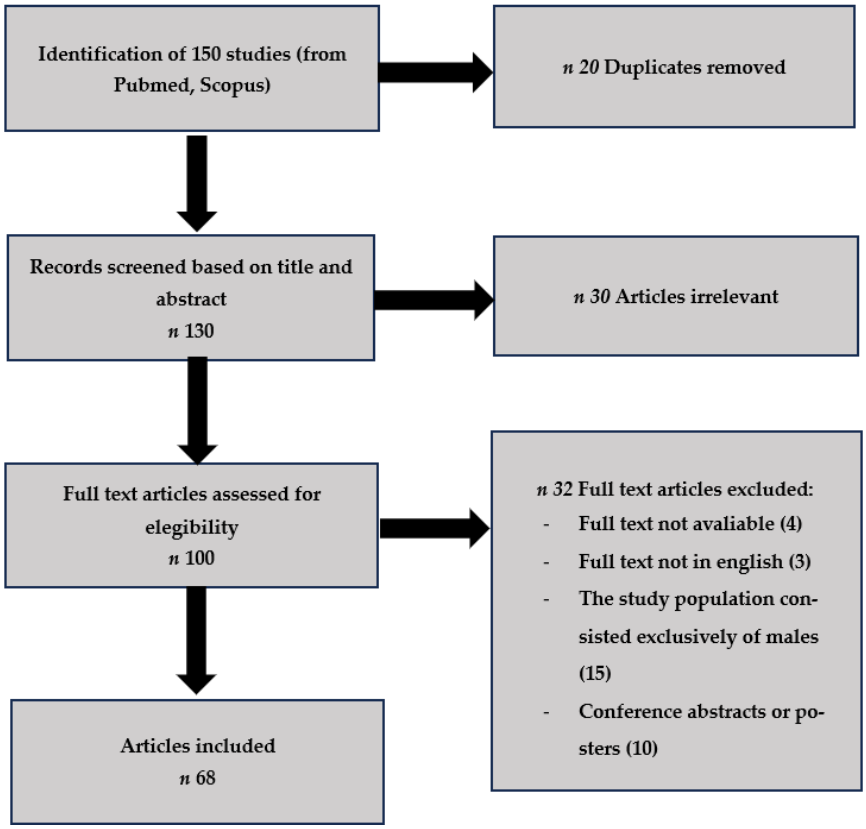

Figure 1. Inclusion criteria diagram.

3.1. Risk Factors During and After Surgical Procedure

Deep vein thrombosis (DVT), pulmonary embolism (PE), and stroke are serious and potentially life-threatening complications that may arise after surgery, particularly following gynecological procedures. Additionally, DVT can significantly reduce the patients' mobility, which in turn impacts their ability to perform daily tasks and lowers their overall quality of life [7]. The most severe outcome of DVT is pulmonary embolism, which carries higher mortality rates and is linked to poorer clinical outcomes [8].

According to various sources, venous thromboembolism (VTE) is recognized as the leading cause of preventable hospital-related deaths [9,10]. It is estimated that VTE is responsible for approximately 500,000 deaths per year in Europe and between 100,000 and 300,000 deaths annually in the United States [11].

Research has indicated that the risk of developing DVT after laparoscopic surgery is comparable to that following traditional gynecological surgery [12]. Hysterectomy is the second most common surgical procedure among women in the United States, with the majority of these surgeries being performed on premenopausal women aged 40 to 44 years [13].

A meta-analysis identified an increased risk of both ischemic and hemorrhagic stroke following oophorectomy, although no such increase was observed in women undergoing hysterectomy alone [14]. In contrast, a UK study found a higher risk of cardiovascular

disease but not stroke [15], likely due to ovarian insufficiency caused by reduced blood supply from the uterine-ovarian ligament [16,17].

A large-scale study in China [18] evaluated the cardiovascular risk in nearly 300,000 premenopausal women (mean age approximately 43 years) who underwent either hysterectomy alone (n = 8478) or hysterectomy with bilateral oophorectomy (n = 1360). This study found no association between these surgeries and hemorrhagic stroke; however, hysterectomy alone was linked to a 6% increased risk of ischemic stroke (adjusted HR 1.06; 1.01–1.10), and hysterectomy with oophorectomy was associated with a 19% increased risk (aHR 1.19; 1.09–1.29). The highest risk of ischemic stroke was observed in women younger than 48 years (hysterectomy alone: HR 1.08; 1.02–1.13, hysterectomy with oophorectomy: HR 1.24; 1.12–1.38), with no significant risk noted in patients older than 48.

Though the study was limited to a select group, the findings suggest that women undergoing these surgeries, especially in the premenopausal stage, should be proactively screened for cardiovascular risk factors and managed accordingly. Further research in more ethnically diverse populations would be beneficial to confirm these results.

There are no reported gender-related differences in anesthetic outcomes. The anesthetic approach—whether for laparoscopic or open surgery, minimally invasive or radical techniques—yields similar outcomes and complication rates for both females and males.

3.2. Risk Factors During Pregnancy and Puerperium

Ischemic stroke (IS) and hemorrhagic stroke (HS) are rare but critical events that can occur during pregnancy and the postpartum period. The incidence of stroke in pregnant women is estimated to be around 30 cases per 100,000 pregnancies [19]. For women with major risk factors like hypertension or pre-eclampsia, the risk can be as much as six times higher [20,21]. Stroke during pregnancy can lead to maternal death or result in severe impairments that affect daily functioning and quality of life.

Between 2011 and 2014, stroke was responsible for 7.4% of maternal deaths in the United States [22]. The occurrence of stroke during pregnancy is on the rise in North America, with Canadian data indicating a 60% increase from 2003 to 2004 to 2015 to 2016 [23,24]. Given that hypertensive disorders of pregnancy contribute to 6.8% of maternal deaths in the U.S., and that stroke is responsible for 40–70% of maternal deaths in pre-eclampsia patients, the true rate of stroke-related maternal mortality is likely underestimated.

Pregnant and postpartum women are susceptible to all types of strokes, with ischemic stroke being the most common. The highest risk periods are the third trimester and the early postpartum phase, especially within the first six weeks after childbirth [25]. Factors that increase stroke risk include advanced maternal age, African American ethnicity, cardiovascular disease, clotting disorders, rheumatological conditions, sickle cell disease, hypertensive pregnancy disorders, gestational diabetes, postpartum hemorrhage, and cesarean section [26,27].

A study conducted in New York found that pre-eclampsia patients who also had infections, chronic hypertension, or clotting disorders were at a consistently high risk of stroke [27]. Pregnancy causes extensive changes to the cardiovascular system, including left atrial enlargement and up to a 35% increase in left ventricular muscle mass, which heightens the risk of ischemic stroke due to cardioembolism [28].

Furthermore, cardiovascular changes during pregnancy make women with a patent foramen ovale more vulnerable to ischemic stroke caused by paradoxical embolism. However, ischemic stroke due to amniotic fluid embolism in patients with a patent foramen ovale (PFO) or pulmonary shunt is rare [29].

A recent systematic review reported a strong link between migraines with aura during pregnancy and an increased risk of ischemic stroke, with odds ratios between 7.9 and 30.7 [30]. However, this connection might be influenced by the difficulty in distinguishing between migraines and severe pre-eclampsia.

Cerebral venous thrombosis (CVT), which involves the formation of clots in the dural sinuses or cortical veins of the brain, can result in venous infarction or hemorrhage. CVT

is commonly seen in the postpartum period, likely due to hypercoagulability and venous stasis, with risk factors including cesarean section, pre-eclampsia, and infections [31]. Symptoms often develop gradually, and medical attention is typically sought only when serious neurological issues or hemorrhage occur. Recent findings suggest that infections (bacterial, fungal, viral, or parasitic) and inflammation can trigger this condition [32–34].

Current estimates indicate that half of all strokes during pregnancy are hemorrhagic [35,36]. Although hemorrhagic strokes can be caused by the rupture of vascular malformations such as arteriovenous malformations (AVMs), cavernous malformations, or cerebral aneurysms, these are less common in pregnant women than in the general population [37,38]. Risk factors for hemorrhagic stroke include hypertensive disorders of pregnancy and coagulation issues, while dural puncture is a very rare cause.

Common symptoms of hemorrhagic stroke include intense headache, changes in consciousness, fainting, and seizures [39].

3.3. Risk Factors During Hormonal Treatment

Women of childbearing age have a lower risk of developing stroke compared to men of the same age or postmenopausal women, likely due to the protective effects of estrogens [40,41]. Endogenous estrogens promote vasodilation, enhance blood flow, and support cell survival by increasing mitochondrial efficiency and stimulating angiogenesis [42]. In women of reproductive age, estrogens are primarily produced by the ovaries, with circulating levels ranging from 40 to 200–400 pg/mL depending on the phase of the menstrual cycle. After menopause, plasma estrogen levels drop to below 20 pg/mL [43]. Hormone replacement therapy (HRT), used to counteract the natural decline in endogenous estrogens, may also have a protective effect on the cardiovascular system. In contrast, the use of oral contraceptives (OCs) reduces the physiological hormonal fluctuations that occur during the menstrual cycle and is associated with an increased risk of developing venous thromboembolism (VTE) [44]. Regarding the association between combined OCs and HRT with stroke, the available studies are fewer and the data more conflicting [45–51]. Some evidence suggests that stroke risk may increase primarily during the first few years of use, while prolonged use might confer a protective effect [48]. This has been attributed to a procoagulant effect early in treatment, which is believed to stabilize over time [52,53]. As a result, the risk of stroke could be offset by the positive impact on atherosclerosis progression [42]. This point is very important because in recent years, the use of estrogen-progestins or progestins as hormone medical therapy has started increasingly earlier. In fact, the recognition of dysmenorrhea in young women as a symptom to be treated since it is often the expression of an organic disease such as endometriosis has meant that hormone therapy has become a medical therapy to be used early and for a long time [54–56]. It is reasonable to assume that women who use OCs or HRT for an extended period may have a similar or even lower risk of stroke compared to those who have never used them. However, studies evaluating the risk of stroke in women who initiate HRT during perimenopause versus later in life have produced conflicting results [57–59]. A recent study [60] demonstrated that both oral contraceptive (OCs) use and oral hormone replacement therapy (HRT) are associated with an increased risk of stroke, particularly during the first year of use. However, the study also found that with continued use of HRT, the heightened stroke risk diminishes over time. The increased incidence of ischemic stroke (IS) during the initial year of use may be attributed to an immediate prothrombotic effect of the therapy [53], which gradually lessens as the body adapts to the hemostatic imbalance over the subsequent period of treatment. In contrast, the underlying mechanism for the immediate increased risk of subarachnoid hemorrhage in patients using hormone replacement therapy (HRT) remains poorly understood. This could potentially be linked to cerebral vasodilation and a transient rise in systemic blood pressure following the initiation of HRT, which might cause the rupture of a pre-existing aneurysm [61,62].

One of the largest studies to date on oral contraceptive (OCs) use and stroke risk was conducted in a Danish cohort of approximately 1.6 million women [46]. This study found a

slightly increased risk of stroke among women who were currently using OCs or had used them for less than a year, but not among those who had used them in the past. However, most of the participants in the study had only used OCs for a short duration, suggesting that the observed increase in stroke risk may be primarily driven by short-term effects. Furthermore, it is important to note that the risk of thromboembolic and ischemic events is closely related to the type and dosage of the drug, as well as the route of administration.

3.4. Modifiable and Non-Modifiable Risk Factors

Stroke, whether ischemic or hemorrhagic, ranks as the second leading cause of death globally [61]. Between 1990 and 2019, stroke prevalence rose by 70%, stroke-related deaths by 43%, and disability-adjusted life years (DALYs) by 32% [63]. Among individuals under 70, both prevalence and incidence rates increased by 22% and 15%, respectively, with national and regional data also showing a rise in stroke rates among younger populations [64–66]. Ischemic events in younger individuals carry a substantial social impact, reducing productive years and increasing the risk of long-term complications, such as recurrent cerebrovascular events. Stroke risk factors can be classified into two categories: those that can be modified and those that cannot. Modifiable factors include hypertension, comorbidities, low physical activity, hyperlipidemia, and, notably, smoking [67]. Smoking has been associated with ischemic stroke in up to 44% of young patients but only around 24% in older adults [68,69]. Furthermore, smoking-related risk is significantly compounded by other factors, such as oral contraceptive use [70,71]. The impact of hypertension is also more pronounced in younger individuals than in older adults [72], likely due to challenges in diagnosing and effectively managing it in younger populations [73]. Studies on obesity as a stroke risk factor have yielded mixed results. Some findings indicate an elevated risk of ischemic stroke among young adults with obesity [74,75], while others find no significant association after accounting for other relevant factors [76]. Dyslipidemia, another critical vascular risk factor, is more frequently observed in men [77,78], though the mechanisms linking lipid profiles to stroke risk are still not fully understood [79]. Cardiovascular risk factors tend to be interrelated, with smoking also contributing to hypertension and hyperlipidemia [80,81]. Each of these factors shows a higher prevalence among men, generally impacting individuals between the ages of 35 and 55 more heavily [82,83]. Young women, on the other hand, face distinct risks such as pregnancy (although evidence suggests it contributes to fewer than 5% of strokes in young women [84,85]), oral contraceptive use, and hormone replacement therapy [86,87]. A recent meta-analysis revealed a dose- and duration-dependent relationship between oral contraceptives and stroke: a 10 μg increase in estrogen dosage and use exceeding five years raised the risk of ischemic stroke (IS) by 20% [88]. Smoking is among the most significant contributors within the category of modifiable risk factors. Smoking is a prevalent habit, notably common among young individuals and in developing nations. [89,90]. Despite the adoption of various policies by governments to reduce smoking rates, the overall number of smokers may not have declined, particularly in relation to population growth in these regions [90]. Data from the Centers for Disease Control and Prevention (CDC) indicate that approximately 20.8% of U.S. adults engage in smoking [91,92]. Although low-nicotine cigarettes are generally seen as less detrimental to health [93], smoking continues to be a major risk factor for strokes. Studies have consistently highlighted a strong dose–response relationship between smoking and the likelihood of ischemic stroke [94,95], likely due to smoking's association with elevated inflammatory markers, which play a role in stroke development [96,97]. A recent meta-analysis [98] found a correlation between smoking and the likelihood of any type of stroke, with current smokers facing a higher stroke risk than non-smokers (OR: 1.46, 95% CI: 1.04–2.07, $p < 0.001$). The analysis indicated that this risk was influenced by sex, with male smokers having an OR of 1.54 (95% CI: 1.11–2.13, $p = 0.002$) and female smokers an OR of 1.88 (95% CI: 1.45–2.44, $p < 0.023$). Among former smokers, the odds ratios were 0.97 (95% CI: 0.68–1.39, $p = 0.025$) for men and 1.18 (95% CI: 0.72–1.92) for women. Additionally, the study found a direct positive correlation between cigarette consumption

and stroke incidence: the risk rose by 12% for every additional 5 cigarettes smoked per day (95% CI: 0.01–0.02, $p < 0.001$). Research indicates no significant correlation between stroke incidence and former smokers, suggesting that quitting smoking positively impacts stroke risk reduction. Additionally, previous studies have shown a strong dose-dependent link between smoking and stroke, particularly among women [99,100]. The meta-analysis also revealed that individuals exposed to secondhand smoke faced a 45% increased overall risk of stroke (OR: 1.45, 95% CI: 1.0–2.11) compared to those unexposed, a difference that was statistically significant ($p < 0.05$). Passive smoking is associated with not only carotid atherosclerosis [101] but also increased levels of homocysteine, fibrinogen, and low-density lipoprotein (LDL) cholesterol [102,103]. Epidemiological studies also reveal that smoking correlates with a heightened risk of sudden cardiac death [85] and atrial fibrillation in a dose-dependent fashion [104]. Other research has linked smoking to diabetes, hypertension, and elevated resting heart rate, which are all contributing risk factors for stroke [105]. Non-modifiable risk factors for stroke include conditions such as patent foramen ovale, migraine with aura, atrial fibrillation, Fabry disease, Moyamoya disease, and connective tissue disorders. Patent foramen ovale (PFO) is a relatively common condition, present in roughly 27% of the general population [106–108]. However, among individuals with cryptogenic stroke, the incidence increases significantly to 62% [70,71]. Similarly, atrial fibrillation (AF) heightens the risk of embolism due to disrupted blood flow [109]. Migraines, particularly with aura, contribute to vascular dysfunction, which increases the likelihood of cardioembolic stroke [110]. This type of migraine is notably more prevalent in young women, whose stroke risk is further amplified by smoking and oral contraceptive use [111,112]. Fabry disease, a lysosomal storage disorder, leads to the thickening of larger blood vessels [113]. Although rare (affecting approximately 1 in 100,000 individuals), stroke occurs in 24–48% of Fabry disease patients, frequently between ages 28 and 54 [114,115]. Moyamoya disease, whose precise cause remains unclear, results in the progressive narrowing of cranial arteries, predominantly affecting individuals under 50 years of age. It is particularly common among urban, low-income populations, with a higher prevalence among people of Asian descent, especially in Japan [116]. Moyamoya disease raises the risk of both ischemic and hemorrhagic strokes [117]. Connective tissue disorders—such as Ehlers-Danlos syndrome, fibromuscular dysplasia, and Marfan syndrome—are also linked to increased stroke risk, as they contribute to vessel fragility [118]. While research is limited, evidence suggests that younger stroke patients more frequently report a family history of stroke than older patients [119]. Findings from the Framingham Heart Study indicate that the risk of ischemic stroke more than doubles among individuals whose parents experienced a stroke before age 65 [120].

A recent systematic review [121] has shown that inherited thrombophilias, including the factor V Leiden mutation, prothrombin G20210A mutation, and protein C and S deficiencies, are significantly associated with an increased risk of arterial ischemic stroke in adults, particularly among younger individuals. The risk is notably higher in patients who are homozygous for these mutations compared to those who are heterozygous. Elevated levels of coagulation proteins, such as factor VIII and factor XI, are also considered independent risk factors for ischemic stroke development [122,123]. In contrast, congenital deficiencies in factors VIII, IX, and XI offer a protective effect against stroke and cardiovascular disease [124]. Anticoagulant therapy has been shown to reduce ischemic stroke risk. Warfarin is non-inferior to aspirin for secondary prevention of noncardioembolic ischemic stroke [125]. While rivaroxaban did not outperform aspirin in preventing recurrence after embolic stroke of undetermined origin [126], combining rivaroxaban with aspirin decreased cardiovascular events, including stroke, in patients with stable atherosclerosis [127]. Although inherited thrombophilias have not been traditionally recognized as risk factors for arterial thrombosis [128], they may contribute to arterial ischemic stroke through several mechanisms. First, ischemic stroke can occur alongside deep vein thrombosis and subsequent paradoxical embolism via a PFO. Second, excessive thrombin activation in individuals with inherited thrombophilia may promote the formation and progression of

atherosclerotic lesions by activating platelets, disrupting endothelial and vascular smooth muscle cells, and recruiting monocytes and macrophages [129].

3.5. Anesthesia Care for Endovascular Thrombectomy

The choice of anesthesia during endovascular thrombectomy (EVT) is a critical factor that can influence procedural success and patient outcomes. The two primary options—monitored anesthesia care (MAC), often referred to as sedation, and general anesthesia (GA)—each come with distinct advantages and disadvantages, influencing the decision-making process in clinical practice [130].

General anesthesia is often favored in scenarios where patient immobility is paramount, such as in those with low Glasgow Coma Scale (GCS) scores. GA provides superior airway control and allows for complete patient immobilization, which is particularly beneficial in complex cases where precision is essential. This level of control can facilitate the smooth coordination of the endovascular team, potentially leading to greater overall satisfaction among the healthcare providers involved [131]. Additionally, GA can reduce the risk of complications during the procedure, such as vessel perforation, thrombus migration, and vascular dissection, which could occur if the patient moves unexpectedly [132]. However, the use of general anesthesia is not without risks. It is more frequently associated with hemodynamic instability, which can complicate the management of the patient both during and after the procedure. Complications arising from mechanical ventilation, such as ventilator-associated pneumonia, are also more common with GA.

On the other hand, monitored anesthesia care offers a different set of benefits. One of the primary advantages of MAC is the shorter time required to initiate the procedure, which is critical in the time-sensitive environment of acute stroke management. Because MAC typically does not involve the use of endotracheal intubation, it is less likely to result in hemodynamic and respiratory disturbances, making it a potentially safer option for patients with unstable cardiovascular status. Additionally, MAC allows for continuous neurological assessment throughout the procedure, enabling real-time evaluation of the patient's condition. This can be crucial for detecting and responding to changes in neurological status immediately. However, one of the significant drawbacks of MAC is the potential for patient movement during the procedure, which can compromise the success of the thrombectomy and increase the risk of procedural complications.

The decision to convert from sedation to general anesthesia during EVT is not uncommon. Flottmann et al. reported a conversion rate of approximately 9.8% [133], while other studies have documented conversion rates as high as 16% [134]. The primary reasons for conversion include severe patient agitation, lack of cooperation, further deterioration in mental status, and the loss of protective airway reflexes. These factors underscore the importance of careful patient selection and close monitoring when choosing MAC for EVT.

3.6. General Anesthesia vs. Monitored Anesthesia Care

Numerous studies have been conducted to compare the outcomes of endovascular thrombectomy performed under general anesthesia versus sedation. One of the landmark trials in this area is the SIESTA trial (Sedation vs. Intubation for Endovascular Stroke Treatment) which found that early outcomes (at 24 h) and functional outcomes at three months were similar between patients who received general anesthesia and those who underwent sedation [135]. This trial provided valuable evidence that both anesthesia approaches can be effective, depending on the specific circumstances of the patient and the procedure.

Further supporting these findings, Sorensen et al. also concluded that the outcomes were comparable between the two anesthesia techniques [136]. In 2022, Maurice et al. published a study in *Anesthesiology* that enrolled 345 patients, comparing their outcomes following EVT under general anesthesia and sedation. They reported that functional outcomes at three months were similar between the two groups. However, they noted

an increased success rate in recanalization in the general anesthesia group, despite longer onset times for the procedures and more frequent hemodynamic disturbances [137].

Zhang et al. focused on patients undergoing thrombectomy for acute anterior circulation ischemic stroke. Their study included 451 patients and found no significant difference in modified Rankin Scale (mRS) scores between the GA and MAC groups at three months post-procedure, further supporting the notion that both approaches can be effective [138].

In the context of posterior circulation thrombectomy, general anesthesia has been more commonly used compared to anterior circulation procedures. The complexity and risks associated with posterior circulation strokes often necessitate the use of GA to ensure patient safety and procedural success. However, some studies have explored the viability of sedation in this setting as well. Liang et al. demonstrated that sedation can result in outcomes comparable to those achieved with general anesthesia, with similar rates of mortality, pulmonary infections, and hemorrhagic transformation, suggesting that MAC may be a viable option even in posterior circulation thrombosis [139]. Geraldini et al. conducted a systematic review and meta-analysis, including nine randomized controlled trials, to compare the effects of general anesthesia and conscious sedation on EVT outcomes. They found no significant differences in functional outcomes at three months between the two anesthesia approaches, further emphasizing that both GA and MAC can be effective depending on the clinical scenario [140]. However, other meta-analyses have provided additional insights. For instance, a comprehensive meta-analysis of 47 studies concluded that general anesthesia was associated with higher rates of successful recanalization and better functional outcomes, but at the cost of an increased risk of post-procedure pneumonia due to prolonged mechanical ventilation [141].

Another meta-analysis, including seven studies published by Campbell et al., summarized the advantages of general anesthesia, particularly in terms of recanalization rates and three-month functional outcomes. The findings from this meta-analysis further underscore the potential benefits of GA, especially in complex or high-risk cases where complete patient immobility is crucial for procedural success [142].

Recent reports indicate some differences in stroke characteristics between males and females. Multiple studies have examined this phenomenon to better understand these findings. Demographic and lifestyle differences are commonly reported; for instance, older females are more likely to live alone than males of the same age. Additionally, females often present for thrombectomy at an older age than males. These factors may contribute to the lower recanalization rates observed in females [143,144]. Interesting findings were reported by Wasiliczuk et al. who investigated gender-based differences in recovery from anesthesia. Their study suggests that females may recover more quickly from anesthesia than males and may also experience a higher incidence of accidental intraoperative awareness. This faster recovery from general anesthesia could be beneficial allowing rapid neurological assessments following thrombectomy [145]. Braithwaite et al. conducted a comprehensive meta-analysis to explore gender-related differences in anesthetic awareness and recovery patterns. Reviewing data from 44 published studies, they observed that females generally demonstrate a faster recovery time following general anesthesia, which they attributed to potential physiological and hormonal differences. Despite this trend, the authors emphasized that these findings are preliminary, and further investigations are necessary to understand the full extent of gender-specific variations in anesthetic response. They called for future studies to account for factors such as hormonal influences, body composition, and metabolic differences, as these may contribute to individualized anesthetic requirements and recovery profiles [146].

The main limitation of the study is the narrative nature, which reduces the degree of recommendation of the proposed treatments. Another limitation is the large time interval of used articles with the inclusion of risk factors typical of more recent times.

The strength of the study is the extensive analysis of all the risk factors that can be assessed to perform an early diagnosis, improving the outcomes of all anesthetic procedures.

4. Conclusions

Early diagnosis is essential for the adequate management of an emergency condition such as stroke. The female population, both due to intrinsic and extrinsic conditions, has an increased risk, so the knowledge of these risk factors allows you to immediately identify the problem. Early diagnosis also allows greater choice in treatment. In fact, choosing an anesthesia technique for endovascular thrombectomy is a significant responsibility that must consider the patient's characteristics and the preferences of the interventional neuroradiologists. While pneumonia risk, prolonged procedure time, and hemodynamic instability are often cited as major concerns, these issues can be mitigated by the experience and skills of the anesthesiologist. With a proficient anesthesia team, the process can be quick, maintaining hemodynamic stability and allowing for extubation immediately after the procedure. Post-procedure pneumonia and hemodynamic instability in these patients are multifactorial. When correctly chosen, the benefits of general anesthesia can outweigh the risks. Ensuring safe and adequate anesthesia care is the anesthesiologist's responsibility. The patient must be immobilized, hemodynamically stable, and have protected airways. Both general anesthesia and local anesthesia are safe approaches, and each should be selected on a case-by-case basis. For posterior circulation thrombosis (basilar system), general anesthesia is mandatory. In cases of anterior circulation thrombosis, if the patient is cooperative and calm, local anesthesia combined with conscious sedation may be an option. General anesthesia is preferable for uncooperative patients or those with low Glasgow Coma Scale (GCS) scores. When properly indicated and performed, general anesthesia is safe and provides better intraoperative conditions for the interventional neuroradiologists, thereby improving success rates.

Author Contributions: Conceptualization. F.C., F.G.M. and E.P.; methodology, R.D., C.d. and A.A.; validation F.C., F.G.M. and E.P.; investigation, C.d., G.D. and K.L.; data curation, F.G.M. and E.P.; writing—original draft preparation F.C., G.H., C.d., A.A. and K.L.; writing—review and editing, F.C., F.G.M., E.P. and G.D.; visualization, R.D., G.H., G.D., A.A. and K.L.; supervision F.C., F.G.M. and E.P. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. World Health Organization. Global Health Estimates: Life Expectancy and Leading Causes of Death and Disability. 2022. Available online: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates (accessed on 3 December 2022). [CrossRef]
2. Mendelson, S.J.; Prabhakaran, S. Diagnosis and management of transient ischemic attack and acute ischemic stroke: A review. *JAMA* **2021**, *325*, 1088–1098. [CrossRef] [PubMed]
3. Fan, Y.; Liao, X.; Pan, Y.; Dong, K.; Wang, Y.; Wang, Y. Thrombolysis Implementation and Monitor of Acute Ischemic Stroke in China (TIMS-China) Investigators. Intravenous Thrombolysis Is Safe and Effective for the Cryptogenic Stroke in China: Data From the Thrombolysis Implementation and Monitor of Acute Ischemic Stroke in China (TIMS-China). *J. Stroke Cerebrovasc. Dis.* **2019**, *28*, 220–226. [CrossRef]
4. Warach, S.J.; Dula, A.N.; Milling, T.J., Jr. Tenecteplase thrombolysis for acute ischemic stroke. *Stroke* **2020**, *51*, 3440–3451. [CrossRef] [PubMed]
5. Mokin, M.; Ansari, S.A.; McTaggart, R.A.; Bulsara, K.R.; Goyal, M.; Chen, M.; Fraser, J.F. Indications for thrombectomy in acute ischemic stroke from emergent large vessel occlusion (ELVO): Report of the SNIS Standards and Guidelines Committee. *J. Neurointerv. Surg.* **2019**, *11*, 215–220. [CrossRef]
6. Kakarla, R.; Vinjavarapu, L.A.; Krishnamurthy, S. Diet and Nutraceutical for treatment and prevention of primary and secondary stroke: Emphasis on nutritional antiplatelet and antithrombotic agents. *Neurochem. Int.* **2024**, *179*, 105823. [CrossRef]

7. Gutzeit, O.; Lauterbach, R.; Loberman, Z.; Sachner, R.; Karram, T.; Lowenstein, L. Laparoscopic sacrocolpopexy complication: Ilio-femoral deep vein thrombosis. *Eur. J. Obstet. Gynecol. Reprod. Biol.* **2020**, *247*, 270–271. [CrossRef]
8. Moragon-Ledesma, S.; Galeano-Valle, F.; Calleja-Carton, E.; Del-Toro-Cervera, J.; Demelo-Rodriguez, P. Bilateral deep vein thrombosis, vena cava agenesis, and renal abnormalities: KILT syndrome—A case report and literature review. *J. Cardiovasc. Transl. Res.* **2020**, *13*, 629–631. [CrossRef]
9. Cohen, A.T.; Tapson, V.F.; Bergmann, J.F.; Goldhaber, S.Z.; Kakkar, A.K.; Deslandes, B. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): A multinational cross-sectional study. *Lancet* **2008**, *371*, 387–394. [CrossRef]
10. American Public Health Association. Advancing awareness to protect patient lives. In Proceedings of the Public Health Leadership Conference on DeepVein Thrombosis, Washington, DC, USA, 26 February 2003; White Paper.
11. The Lancet Haematology. Thromboembolism: An under appreciated cause of death. *Lancet Haematol.* **2015**, *2*, e393. [CrossRef] [PubMed]
12. Chong, W.; Bui, A.H.; Menhaji, K. Incidence and risk factors for venous thromboembolism events after different routes of pelvic organ prolapse repairs. *Am. J. Obstet. Gynecol.* **2020**, *223*, 268.e1–268.e26. [CrossRef]
13. Whiteman, M.K.; Hillis, S.D.; Jamieson, D.J.; Morrow, B.; Podgornik, M.N.; Brett, K.M.; Marchbanks, P.A. Inpatient hysterectomy surveillance in the United States, 2000–2004. *Am. J. Obstet. Gynecol.* **2008**, *198*, 34.e1–34.e7. [CrossRef]
14. Poorthuis, M.H.; Algra, A.M.; Algra, A.; Kappelle, L.J.; Klijn, C.J. Female- and Male-Specific Risk Factors for Stroke: A Systematic Review and Meta-analysis. *JAMA Neurol.* **2017**, *74*, 75–81. [CrossRef] [PubMed]
15. Peters, S.A.; Woodward, M. Women's reproductive factors and incident cardiovascular disease in the UK Biobank. *Heart* **2018**, *104*, 1069–1075. [CrossRef] [PubMed]
16. Moorman, P.G.; Myers, E.R.; Schildkraut, J.M.; Iversen, E.S.; Wang, F.; Warren, N. Effect of hysterectomy with ovarian preservation on ovarian function. *Obstet. Gynecol.* **2011**, *118*, 1271–1279. [CrossRef] [PubMed]
17. Trabuco, E.C.; Moorman, P.G.; Algeciras-Schimnich, A.; Weaver, A.L.; Cliby, W.A. Association of ovary-sparing hysterectomy with ovarian reserve. *Obstet. Gynecol.* **2016**, *127*, 819–827. [CrossRef] [PubMed]
18. Poorthuis, M.H.F.; Yao, P.; Chen, Y.; Guo, Y.; Shi, L.; Li, L.; Chen, Z.; Clarke, R.; Yang, L.; China Kadoorie Biobank Collaborative Group. Risks of Stroke and Heart Disease Following Hysterectomy and Oophorectomy in Chinese Premenopausal Women. *Stroke* **2022**, *53*, 3064–3071. [CrossRef] [PubMed]
19. Swartz, R.H.; Cayley, M.L.; Foley, N.; Ladhani, N.N.N.; Leffert, L.; Bushnell, C.; McClure, J.A.; Lindsay, M.P. The incidence of pregnancy-related stroke: A systematic review and meta-analysis. *Int. J. Stroke* **2017**, *12*, 687–697. [CrossRef] [PubMed]
20. Kittner, S.J.; Stern, B.J.; Feeser, B.R.; Hebel, J.R.; Nagey, D.A.; Buchholz, D.W.; Earley, C.J.; Johnson, C.J.; Macko, R.F.; Sloan, M.A.; et al. Pregnancy and the risk of stroke. *N. Engl. J. Med.* **1996**, *335*, 768–774. [CrossRef] [PubMed]
21. Crovetto, F.; Somigliana, E.; Peguero, A.; Figueras, F. Stroke during pregnancy and pre-eclampsia. *Curr. Opin. Obstet. Gynecol.* **2013**, *25*, 425–432. [CrossRef] [PubMed]
22. *Pregnancy Mortality Surveillance System*; Centers for Disease Control and Prevention: Atlanta, GA, USA, 2017.
23. Kuklina, E.V.; Tong, X.; Bansil, P.; George, M.G.; Callaghan, W.M. Trends in pregnancy hospitalizations that included a stroke in the United States from 1994 to 2007: Reasons for concern? *Stroke* **2011**, *42*, 2564–2570. [CrossRef] [PubMed]
24. Liu, S.; Chan, W.-S.; Ray, J.G.; Kramer, M.S.; Joseph, K.S. Stroke and cerebrovascular disease in pregnancy. *Stroke* **2019**, *50*, 13–20. [CrossRef]
25. van Alebeek, M.E.; de Heus, R.; Tuladhar, A.M.; de Leeuw, F.E. Pregnancy and ischemic stroke: A practical guide to management. *Curr. Opin. Neurol.* **2018**, *31*, 44–51. [CrossRef] [PubMed]
26. Scott, C.A.; Bewley, S.; Rudd, A.; Spark, P.; Kurinczuk, J.J.; Brocklehurst, P.; Knight, M. Incidence, risk factors, management, and outcomes of stroke in pregnancy. *Obstet. Gynecol.* **2012**, *120*, 318–324. [CrossRef] [PubMed]
27. Miller, E.C.; Gatollari, H.J.; Too, G.; Boehme, A.K.; Leffert, L.; Marshall, R.S.; Elkind, M.S.; Willey, J.Z. Risk factors for pregnancy-associated stroke in women with preeclampsia. *Stroke* **2017**, *48*, 1752–1759. [CrossRef] [PubMed]
28. Hasegawa, J.; Ikeda, T.; Sekizawa, A.; Tanaka, H.; Nakata, M.; Murakoshi, T.; Katsuragi, S.; Osato, K.; Ishiwata, I.; Kinoshita, K.; et al. Maternal death due to stroke associated with pregnancy-induced hypertension. *Circ. J.* **2015**, *79*, 1835–1840. [CrossRef] [PubMed]
29. Melchiorre, K.; Sharma, R.; Khalil, A.; Thilaganathan, B. Maternal cardiovascular function in normal pregnancy: Evidence of maladaptation to chronic volume overload. *Hypertension.* **2016**, *67*, 754762. [CrossRef] [PubMed]
30. Wabnitz, A.; Bushnell, C. Migraine, cardiovascular disease, and stroke during pregnancy: Systematic review of the literature. *Cephalalgia* **2015**, *35*, 132–139. [CrossRef] [PubMed]
31. Lanska, D.J.; Kryscio, R.J. Risk factors for peripartum and postpartum stroke and intracranial venous thrombosis. *Stroke* **2000**, *31*, 1274–1282. [CrossRef] [PubMed]
32. Esenwa, C.C.; Elkind, M.S. Inflammatory risk factors, biomarkers and associated therapy in ischaemic stroke. *Nat. Rev. Neurol.* **2016**, *12*, 594–604. [CrossRef] [PubMed]
33. Gao, H.; Yang, B.J.; Jin, L.P.; Jia, X.F. Predisposing factors, diagnosis, treatment and prognosis of cerebral venous thrombosis during pregnancy and postpartum: A case-control study. *Chin. Med. J.* **2011**, *124*, 4198–4204. [PubMed]
34. James, A.H.; Bushnell, C.D.; Jamison, M.G.; Myers, E.R. Incidence and risk factors for stroke in pregnancy and the puerperium. *Obstet. Gynecol.* **2005**, *106*, 509–516. [CrossRef] [PubMed]

35. Leffert, L.R.; Clancy, C.R.; Bateman, B.T.; Cox, M.; Schulte, P.J.; Smith, E.E.; Fonarow, G.C.; Schwamm, L.H.; Kuklina, E.V.; George, M.G.; et al. Patient characteristics and outcomes after hemorrhagic stroke in pregnancy. *Circ. Cardiovasc. Qual. Outcomes* **2015**, *8*, S170–S178. [CrossRef] [PubMed]
36. Bateman, B.T.; Schumacher, H.C.; Bushnell, C.D.; Pile-Spellman, J.; Simpson, L.L.; Sacco, R.L.; Berman, M.F. Intracerebral hemorrhage in pregnancy: Frequency, risk factors, and outcome. *Neurology* **2006**, *67*, 424–429. [CrossRef] [PubMed]
37. Bateman, B.T.; Olbrecht, V.A.; Berman, M.F.; Minehart, R.D.; Schwamm, L.H.; Leffert, L.R. Peripartum subarachnoid hemorrhage: Nationwide data and institutional experience. *Anesthesiology* **2012**, *116*, 324–333. [CrossRef] [PubMed]
38. Sharshar, T.; Lamy, C.; Mas, J.L. Incidence and causes of strokes associated with pregnancy and puerperium. A study in public hospitals of Ile de France. Stroke Pregnancy Study Group. *Stroke* **1995**, *26*, 930–936. [CrossRef] [PubMed]
39. Eggert, S.M.; Eggers, K.A. Subarachnoid haemorrhage following spinal anaesthesia in an obstetric patient. *Br. J. Anaesth.* **2001**, *86*, 442–444. [CrossRef] [PubMed]
40. Persky, R.W.; Turtzo, L.C.; McCullough, L.D. Stroke in women: Disparities and outcomes. *Curr. Cardiol. Rep.* **2010**, *12*, 6–13. [CrossRef]
41. Paganini-Hill, A. Hormone replacement therapy and stroke: Risk, protection or no effect? *Maturitas* **2001**, *38*, 243–261. [CrossRef]
42. Krause, D.N.; Duckles, S.P.; Pelligrino, D.A. Influence of sex steroid hormones on cerebrovascular function. *J. Appl. Physiol. (1985)* **2006**, *101*, 1252–1261. [CrossRef]
43. Taylor, H.S.; Pal, L.; Seli, E. *Clinical Gynecologic Endocrinology and Infertility*; Wolters Kluwer Health: Philadelphia, PA, USA, 2019.
44. John, S.; Jacobi, J.; Schlaich, M.P.; Delles, C.; Schmieder, R.E. Effects of oral contraceptives on vascular endothelium in premenopausal women. *Am. J. Obstet. Gynecol.* **2000**, *183*, 28–33. [CrossRef]
45. Weill, A.; Dalichampt, M.; Raguideau, F.; Ricordeau, P.; Blotière, P.O.; Rudant, J.; Alla, F.; Zureik, M. Low dose oestrogen combined oral contraception and risk of pulmonary embolism, stroke, and myocardial infarction in five million French women: Cohort study. *BMJ* **2016**, *353*, i2002. [CrossRef] [PubMed]
46. Lidegaard, Ø.; Løkkegaard, E.; Jensen, A.; Skovlund, C.W.; Keiding, N. Thrombotic stroke and myocardial infarction with hormonal contraception. *N. Engl. J. Med.* **2012**, *366*, 2257–2266. [CrossRef] [PubMed]
47. Stampfer, M.J.; Willett, W.C.; Colditz, G.A.; Speizer, F.E.; Hennekens, C.H. A prospective study of past use of oral contraceptive agents and risk of cardiovascular diseases. *N. Engl. J. Med.* **1988**, *319*, 1313–1317. [CrossRef] [PubMed]
48. Viscoli, C.M.; Brass, L.M.; Kernan, W.N.; Sarrel, P.M.; Suissa, S.; Horwitz, R.I. A clinical trial of estrogen-replacement therapy after ischemic stroke. *N. Engl. J. Med.* **2001**, *345*, 1243–1249. [CrossRef]
49. Løkkegaard, E.; Jovanovic, Z.; Heitmann, B.L.; Keiding, N.; Ottesen, B.; Hundrup, Y.A.; Obel, E.B.; Pedersen, A.T. Increased risk of stroke in hypertensive women using hormone therapy: Analyses based on the Danish Nurse Study. *Arch. Neurol.* **2003**, *60*, 1379–1384. [CrossRef]
50. Grodstein, F.; Manson, J.E.; Colditz, G.A.; Willett, W.C.; Speizer, F.E.; Stampfer, M.J. A prospective, observational study of postmenopausal hormone therapy and primary prevention of cardiovascular disease. *Ann. Intern. Med.* **2000**, *133*, 933–941. [CrossRef]
51. Lemaitre, R.N.; Weiss, N.S.; Smith, N.L.; Psaty, B.M.; Lumley, T.; Larson, E.B.; Heckbert, S.R. Esterified estrogen and conjugated equine estrogen and the risk of incident myocardial infarction and stroke. *Arch. Intern. Med.* **2006**, *166*, 399–404. [CrossRef]
52. Prentice, R.L.; Langer, R.D.; Stefanick, M.L.; Howard, B.V.; Pettinger, M.; Anderson, G.L.; Barad, D.; Curb, J.D.; Kotchen, J.; Kuller, L.; et al. Combined analysis of Women's Health Initiative observational and clinical trial data on postmenopausal hormone treatment and cardiovascular disease. *Am. J. Epidemiol.* **2006**, *163*, 589–599. [CrossRef]
53. Rosendaal, F.R.; Helmerhorst, F.M.; Vandenbroucke, J.P. Female hormones and thrombosis. *Arter. Thromb. Vasc. Biol.* **2002**, *22*, 201–210. [CrossRef] [PubMed]
54. Martire, F.G.; Piccione, E.; Exacoustos, C.; Zupi, E. Endometriosis and adolescence: The impact of dysmenorrhea. *J. Clin. Med.* **2023**, *12*, 5624. [CrossRef] [PubMed]
55. Martire, F.G.; Giorgi, M.; D'Abate, C.; Colombi, C.; Ginetti, A.; Cannoni, A.; Fedele, F.; Exacoustos, C.; Centini, G.; Zupi, E.; et al. Deep infiltrating endometriosis in adolescence: Early diagnosis and possible prevention of disease progression. *J. Clin. Med.* **2024**, *13*, 550. [CrossRef]
56. Becker, C.M.; Bokor, A.; Heikinheimo, O.; Horne, A.; Jansen, F.; Kiesel, L.; King, K.; Kvaskoff, M.; Nap, A.; Petersen, K.; et al. ESHRE guideline: Endometriosis. *Human. Reprod. Open* **2022**, *2022*, hoac009. [CrossRef]
57. Clarkson, T.B. Estrogen effects on arteries vary with stage of reproductive life and extent of subclinical atherosclerosis progression. *Menopause* **2007**, *14 Pt 1*, 373–384. [CrossRef]
58. Smoller, S.; Hendrix, S.L.; Limacher, M.; Heiss, G.; Kooperberg, C.; Baird, A.; Kotchen, T.; Curb, J.D.; Black, H.; Rossouw, J.E.; et al. Effect of estrogen plus progestin on stroke in postmenopausal women: The Women's Health Initiative: A randomized trial. *JAMA* **2003**, *289*, 2673–2684. [CrossRef]
59. Grodstein, F.; Manson, J.E.; Stampfer, M.J.; Rexrode, K. Postmenopausal hormone therapy and stroke: Role of time since menopause and age at initiation of hormone therapy. *Arch. Intern. Med.* **2008**, *168*, 861–866. [CrossRef]
60. Johansson, T.; Fowler, P.; Ek, W.E.; Skalkidou, A.; Karlsson, T.; Johansson, Å. Oral Contraceptives, Hormone Replacement Therapy, and Stroke Risk. *Stroke* **2022**, *53*, 3107–3115. [CrossRef]
61. Bain, C.A.; Walters, M.R.; Lees, K.R.; Lumsden, M.A. The effect of HRT on cerebral haemodynamics and cerebral vasomotor reactivity in post-menopausal women. *Hum. Reprod.* **2004**, *19*, 2411–2414. [CrossRef]

62. Tuomikoski, P.; Haapalahti, P.; Sarna, S.; Ylikorkala, O.; Mikkola, T.S. Vasomotor hot flushes and 24-hour ambulatory blood pressure in normotensive women: A placebo-controlled trial on post-menopausal hormone therapy. *Ann. Med.* **2010**, *42*, 334–343. [CrossRef]
63. GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol.* **2021**, *20*, 795–820. [CrossRef]
64. Béjot, Y.; Delpont, B.; Giroud, M. Rising stroke incidence in young adults: More epidemiological evidence, more questions to be answered. *J. Am. Heart Assoc.* **2016**, *5*, e003661. [CrossRef] [PubMed]
65. Bako, A.T.; Pan, A.; Potter, T.; Tannous, J.; Johnson, C.; Baig, E.; Meeks, J.; Woo, D.; Vahidy, F.S. Contemporary trends in the nationwide incidence of primary intracerebral hemorrhage. *Stroke* **2022**, *53*, e70–e74. [CrossRef] [PubMed]
66. Boot, E.; Ekker, M.S.; Putaala, J.; Kittner, S.; De Leeuw, F.-E.; Tuladhar, A.M. Ischaemic stroke in young adults: A global perspective. *J. Neurol. Neurosurg. Psychiatry* **2020**, *91*, 411–417. [CrossRef]
67. George, M.G. Risk factors for ischemic stroke in younger adults. *Stroke* **2020**, *51*, 729–735. [CrossRef]
68. Parikh, N.S.; Chatterjee, A.; Díaz, I.; Merkler, A.E.; Murthy, S.B.; Iadecola, C.; Navi, B.B.; Kamel, H. Trends in active cigarette smoking among stroke survivors in the United States, 1999 to 2018. *Stroke* **2020**, *51*, 1656–1661. [CrossRef] [PubMed]
69. Markidan, J.; Cole, J.W.; Cronin, C.A.; Merino, J.G.; Phipps, M.S.; Wozniak, M.A.; Kittner, S.J. Smoking and risk of ischemic stroke in young men. *Stroke* **2018**, *49*, 1276–1278. [CrossRef] [PubMed]
70. Pezzini, A.; Grassi, M.; Lodigiani, C.; Patella, R.; Gandolfo, C.; Casoni, F.; Musolino, R.; Calabrò, R.S.; Bovi, P.; Adami, A.; et al. Predictors of migraine subtypes in young adults with ischemic stroke: The Italian project on stroke in young adults. *Stroke* **2011**, *42*, 17–21. [CrossRef]
71. MacClellan, L.R.; Giles, W.; Cole, J.; Wozniak, M.; Stern, B.; Mitchell, B.D.; Kittner, S.J. Probable migraine with visual aura and risk of ischemic stroke: The stroke prevention in young women study. *Stroke* **2007**, *38*, 2438–2445. [CrossRef]
72. Roger, V.L.; Go, A.S.; Lloyd-Jones, D.M.; Benjamin, E.J.; Berry, J.D.; Borden, W.B.; Bravata, D.M.; Dai, S.; Ford, E.S.; Fox, C.S. Heart disease and stroke statistics—2012 update: A report from the American Heart Association. *Circulation* **2012**, *125*, e2–e220.
73. Mszar, R.; Mahajan, S.; Valero-Elizondo, J.; Yahya, T.; Sharma, R.; Grandhi, G.R.; Khera, R.; Virani, S.S.; Lichtman, J.; Khan, S.U. Association between sociodemographic determinants and disparities in stroke symptom awareness among US young adults. *Stroke* **2020**, *51*, 3552–3561. [CrossRef] [PubMed]
74. Bardugo, A.; Fishman, B.; Libruder, C.; Tanne, D.; Ram, A.; Hershkovitz, Y.; Zucker, I.; Furer, A.; Gilon, R.; Chodick, G.; et al. Body mass index in 1.9 million adolescents and stroke in young adulthood. *Stroke* **2021**, *52*, 2043–2052. [CrossRef]
75. Mitchell, A.B.; Cole, J.W.; McArdle, P.F.; Cheng, Y.-C.; Ryan, K.A.; Sparks, M.J.; Mitchell, B.D.; Kittner, S.J. Obesity increases risk of ischemic stroke in young adults. *Stroke* **2015**, *46*, 1690–1692. [CrossRef] [PubMed]
76. Sultan, S.; Elkind, M.S.V. The growing problem of stroke among young adults. *Curr. Cardiol. Rep.* **2013**, *15*, 421. [CrossRef] [PubMed]
77. Menet, R.; Bernard, M.; ElAli, A. Hyperlipidemia in stroke pathobiology and therapy: Insights and perspectives. *Front. Physiol.* **2018**, *9*, 488. [CrossRef] [PubMed]
78. Talpur, M.T.H.; Katbar, M.T.; Shabir, K.U.; Shabir, K.U.; Yaqoob, U.; Jabeen, S.; Zia, D. Prevalence of dyslipidemia in young adults. *Prof. Med. J.* **2020**, *27*, 987–993. [CrossRef]
79. Yin, R.; Wu, J.; Lin, W.; Chen, Y.; Yang, D.; Pan, S. The environmental and genetic evidence for the association of hyperlipidemia and hypertension. *J. Hypertens.* **2009**, *27*, 251–258.
80. Gialeraki, A.; Valsami, S.; Pittaras, T.; Panayiotakopoulos, G.; Politou, M. Oral contraceptives and HRT risk of thrombosis. *Clin. Appl. Thromb. Hemost.* **2018**, *24*, 217–225. [CrossRef] [PubMed]
81. Li, F.; Zhu, L.; Zhang, J.; He, H.; Qin, Y.; Cheng, Y.; Xie, Z. Oral contraceptive use and increased risk of stroke: A dose–response metaanalysis of observational studies. *Front. Neurol.* **2019**, *10*, 993. [CrossRef] [PubMed]
82. Maaijwee, N.A.M.M.; Rutten-Jacobs, L.C.A.; Schaapsmeerders, P.; van Dijk, E.J.; de Leeuw, F.-E. Ischaemic stroke in young adults: Risk factors and long-term consequences. *Nat. Rev. Neurol.* **2014**, *10*, 315–325. [CrossRef]
83. Putaala, J.; Yesilot, N.; Waje-Andreassen, U.; Pitkäniemi, J.; Vassilopoulou, S.; Nardi, K.; Odier, C.; Hofgart, G.; Engelter, S.; Burow, A.; et al. Demographic and geographic vascular risk factor differences in European young adults with ischemic stroke: The 15 cities young stroke study. *Stroke* **2012**, *43*, 2624–2630. [CrossRef]
84. Putaala, J.; Metso, A.J.; Metso, T.M.; Konkola, N.; Kraemer, Y.; Haapaniemi, E.; Kaste, M.; Tatlisumak, T. Analysis of 1008 consecutive patients aged 15 to 49 with first-ever ischemic stroke: The Helsinki young stroke registry. *Stroke* **2009**, *40*, 1195–1203. [CrossRef]
85. Ekker, M.S.; Verhoeven, J.I.; Vaartjes, I.; van Nieuwenhuizen, K.M.; Klijn, C.J.M.; de Leeuw, F.-E. Stroke incidence in young adults according to age, subtype, sex, and time trends. *Neurology* **2019**, *92*, e2444–e2454. [CrossRef] [PubMed]
86. Arnao, V.; Acciarresi, M.; Cittadini, E.; Caso, V. Stroke incidence, prevalence and mortality in women worldwide. *Int. J. Stroke* **2016**, *11*, 287–301. [CrossRef]
87. Ng, M.; Freeman, M.K.; Fleming, T.D.; Robinson, M.; Dwyer-Lindgren, L.; Thomson, B.; Wollum, A.; Sanman, E.; Wulf, S.; Lopez, A.D.; et al. Smoking prevalence and cigarette consumption in 187 countries, 1980–2012. *JAMA* **2014**, *311*, 183–192. [CrossRef] [PubMed]

88. Sreeramareddy, C.T.; Pradhan, P.M.; Mir, I.A.; Sin, S. Smoking and smokeles tobacco use in nine South and Southeast Asian countries: Prevalence estimates and social determinants from Demographic and Health Surveys. *Popul. Health Metr.* **2014**, *12*, 22–48. [CrossRef] [PubMed]
89. Feigin, V.L.; Roth, G.A.; Naghavi, M.; Parmar, P.; Krishnamurthi, R.; Chugh, S.; Mensah, G.A.; Norrving, B.; Shiue, I.; Ng, M.; et al. Global burden of stroke an risk factors in 188 countries, during 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol.* **2016**, *15*, 913–924. [CrossRef] [PubMed]
90. Denlinger-Apte, R.L.; Joel, D.L.; Strasser, A.A.; Donny, E.C. Low nicotine content descriptors reduce perceived health risks and positive cigarette ratings in participants using very low nicotine content cigarettes. *Nicotine Tob. Res.* **2017**, *19*, 1149–1154. [CrossRef]
91. Thrift, A.G.; Thayabaranathan, T.; Howard, G.; Howard, V.J.; Rothwell, P.M.; Feigin, V.L.; Norrving, B.; Donnan, G.A.; Cadilhac, D.A. Global stroke statistics. *Int. J. Stroke* **2017**, *12*, 13–32. [CrossRef]
92. Kwan, J.H.G.; Bryant, T. IL-6 is a predictive biomarker for stroke associated infection and future mortality in the elderly after an ischemic stroke. *Exp. Gerontol.* **2013**, *48*, 960–965. [CrossRef]
93. Tuttolomondo, A.; Di Sciacca, R.; Di Raimondo, D.; Pedone, C.; La Placa, S.; Pinto, A.; Licata, G. Effects of clinical and laboratory variables and of pretreatment with cardiovascular drugs in acute ischaemic stroke: A retrospective chart review from the GIFA study. *Int. J. Cardiol.* **2011**, *151*, 318–322. [CrossRef]
94. Pan, B.; Jin, X.; Jun, L.; Qiu, S.; Zheng, Q.; Pan, M. The relationship between smoking and stroke: A meta-analysis. *Medicine* **2019**, *98*, e14872. [CrossRef]
95. Ruth Bonita Meir, J. Cigarette smoking and risk of stroke in middle-aged women. *N. Engl. J. Med.* **1988**, *318*, 937–941.
96. Bhat, V.M.; Cole, J.W.; Sorkin, J.D.; Wozniak, M.A.; Malarcher, A.M.; Giles, W.H.; Stern, B.J.; Kittner, S.J. Dose-response relationship between cigarette smoking and risk of ischemic stroke in young women. *Stroke* **2008**, *39*, 2439–2443. [CrossRef] [PubMed]
97. Hackshaw, A.; Morris, J.K.; Boniface, S.; Tang, J.-L.; Milenković, D. Low cigarette consumption and risk of coronary heart disease and stroke: Meta-analysis of 141 cohort studies in 55 study reports. *BMJ* **2018**, *360*, j5855. [CrossRef]
98. Bowman, T.S.; Gaziano, J.M.; Buring, J.E.; Sesso, H.D. A prospective study of cigarette smoking and risk of incident hypertension in women. *J. Am. Coll. Cardiol.* **2007**, *50*, 2085–2092. [CrossRef] [PubMed]
99. Rehill, N.; Beck, C.R.; Yeo, K.R.; Yeo, W.W. The effect of chronic tobacco smoking on arterial stiffness. *Br. J. Clin. Pharmacol.* **2006**, *61*, 767–773. [CrossRef] [PubMed]
100. Panagiotakos, D.B.; Pitsavos, C.; Chrysohoou, C.; Skoumas, J.; Masoura, C.; Toutouzas, P.; Stefanadis, C.; ATTICA Study. Effect of exposure to secondhand smoke on markers of inflammation: The ATTICA study. *Am. J. Med.* **2004**, *116*, 145–150. [CrossRef] [PubMed]
101. Aune, D.; Schlesinger, S.; Norat, T.; Riboli, E. Tobacco smoking and the risk of sudden cardiac death: A systematic review and meta-analysis of prospective studies. *Eur. J. Epidemiol.* **2018**, *33*, 509–521. [CrossRef] [PubMed]
102. Aune, D.; Schlesinger, S.; Norat, T.; Riboli, E. Tobacco smoking and the risk of atrial fibrillation: A systematic review and meta-analysis of prospective studies. *Eur. J. Prev. Cardiol.* **2018**, *25*, 1437–1451. [CrossRef]
103. Akter, S.; Goto, A.; Mizoue, T. Smoking and the risk of type 2 diabetes in Japan: A systematic review and meta-analysis. *J. Epidemiol.* **2017**, *27*, 553–561. [CrossRef]
104. Kent, D.M.; Ruthazer, R.; Weimar, C.; Mas, J.-L.; Serena, J.; Homma, S.; Di Angelantonio, E.; Di Tullio, M.R.; Lutz, J.S.; Elkind, M.S.; et al. An index to identify stroke-related vs incidental patent foramen ovale in cryptogenic stroke. *Neurology* **2013**, *81*, 619–625. [CrossRef]
105. Nedeltchev, K.; Wiedmer, S.; Schwerzmann, M.; Windecker, S.; Haefeli, T.; Meier, B.; Mattle, H.P.; Arnold, M. Sex differences in cryptogenic stroke with patent foramen ovale. *Am. Heart J.* **2008**, *156*, 461–465. [CrossRef] [PubMed]
106. Yahya, T.; Jilani, M.H.; Khan, S.U.; Mszar, R.; Hassan, S.Z.; Blaha, M.J.; Blankstein, R.; Virani, S.S.; Johansen, M.C.; Vahidy, F.; et al. Stroke in young adults: Current trends, opportunities for prevention and pathways forward. *Am. J. Prev. Cardiol.* **2020**, *3*, 100085. [CrossRef] [PubMed]
107. Handke, M.; Harloff, A.; Olschewski, M.; Hetzel, A.; Geibel, A. Patent foramen ovale and cryptogenic stroke in older patients. *N. Engl. J. Med.* **2007**, *357*, 2262–2268. [CrossRef] [PubMed]
108. Kamel, H.; Okin, P.M.; Elkind, M.S.V.; Iadecola, C. Atrial fibrillation and mechanisms of stroke: Time for a new model. *Stroke* **2016**, *47*, 895–900. [CrossRef] [PubMed]
109. Øie, L.R.; Kurth, T.; Gulati, S.; Dodick, D.W. Migraine and risk of stroke. *J. Neurol. Neurosurg. Psychiatry* **2020**, *91*, 593–604. [CrossRef]
110. Ortiz, A.; Germain, D.P.; Desnick, R.J.; Politei, J.; Mauer, M.; Burlina, A.; Eng, C.; Hopkin, R.J.; Laney, D.; Linhart, A.; et al. Fabry disease revisited: Management and treatment recommendations for adult patients. *Mol. Genet. Metab.* **2018**, *123*, 416–427. [CrossRef]
111. Kolodny, E.; Fellgiebel, A.; Hilz, M.J.; Sims, K.; Caruso, P.; Phan, T.G.; Politei, J.; Manara, R.; Burlina, A. Cerebrovascular involvement in Fabry disease: Current status of knowledge. *Stroke* **2015**, *46*, 302–313. [CrossRef]
112. Buechner, S.; Moretti, M.; Burlina, A.P.; Cei, G.; Manara, R.; Ricci, R.; Mignani, R.; Parini, R.; Di Vito, R.; Giordano, G.P.; et al. Central nervous system involvement in Anderson-Fabry disease: A clinical and MRI retrospective study. *J. Neurol. Neurosurg. Psychiatry* **2008**, *79*, 1249–1254. [CrossRef]

113. Ghaffari-Rafi, A.; Ghaffari-Rafi, S.; Leon-Rojas, J. Socioeconomic and demographic disparities of moyamoya disease in the United States. *Clin. Neurol. Neurosurg.* **2020**, *192*, 105719. [CrossRef]
114. Burke, G.M.; Burke, A.M.; Sherma, A.K.; Hurley, M.C.; Batjer, H.H.; Bendok, B.R. Moyamoya disease: A summary. *Neurosurg. Focus.* **2009**, *26*, E11. [CrossRef]
115. Yasaka, M.; Minematsu, K. Stroke in young adults in Japan. *Rinsho Shinkeigaku* **2005**, *45*, 842–845. [PubMed]
116. Vanakker, O.M.; Hemelsoet, D.; De Paepe, A. Hereditary connective tissue diseases in young adult stroke: A comprehensive synthesis. *Stroke Res. Treat.* **2011**, *2011*, 712903. [CrossRef] [PubMed]
117. Cheng, Y.-C.; Cole, J.W.; Kittner, S.J.; Mitchell, B.D. Genetics of ischemic stroke in young adults. *Circ. Cardiovasc. Genet.* **2014**, *7*, 383–392. [CrossRef] [PubMed]
118. Seshadri, S.; Beiser, A.; Pikula, A.; Himali, J.J.; Kelly-Hayes, M.; Debette, S.; DeStefano, A.L.; Romero, J.R.; Kase, C.S.; Wolf, P.A. Parental occurrence of stroke and risk of stroke in their children: The Framingham study. *Circulation* **2010**, *121*, 1304–1312. [CrossRef] [PubMed]
119. Chiasakul, T.; De Jesus, E.; Tong, J.; Chen, Y.; Crowther, M.; Garcia, D.; Chai-Adisaksopha, C.; Messé, S.R.; Cuker, A. Inherited Thrombophilia and the Risk of Arterial Ischemic Stroke: A Systematic Review and Meta-Analysis. *J. Am. Heart Assoc.* **2019**, *8*, e012877. [CrossRef] [PubMed]
120. Suri, M.F.; Yamagishi, K.; Aleksic, N.; Hannan, P.J.; Folsom, A.R. Novel hemostatic factor levels and risk of ischemic stroke: The Atherosclerosis Risk in Communities (ARIC) study. *Cerebrovasc. Dis.* **2010**, *29*, 497–502. [CrossRef]
121. Zakai, N.A.; Judd, S.E.; Kissela, B.; Howard, G.; Safford, M.M.; Cushman, M. Factor VIII, protein C and cardiovascular disease risk: The reasons for geographic and racial differences in stroke study (REGARDS). *Thromb. Haemost.* **2018**, *118*, 1305–1315. [CrossRef]
122. Salomon, O.; Steinberg, D.M.; Koren-Morag, N.; Tanne, D.; Seligsohn, U. Reduced incidence of ischemic stroke in patients with severe factor XI deficiency. *Blood* **2008**, *111*, 4113–4117. [CrossRef]
123. Sood, S.L.; Cheng, D.; Ragni, M.; Kessler, C.M.; Quon, D.; Shapiro, A.D.; Key, N.S.; Manco-Johnson, M.J.; Cuker, A.; Kempton, C.; et al. A cross-sectional analysis of cardiovascular disease in the hemophilia population. *Blood Adv.* **2018**, *2*, 1325–1333. [CrossRef]
124. Mohr, J.P.; Thompson, J.L.; Lazar, R.M.; Levin, B.; Sacco, R.L.; Furie, K.L.; Kistler, J.P.; Albers, G.W.; Pettigrew, L.C.; Adams, H.P., Jr.; et al. A comparison of warfarin and aspirin for the prevention of recurrent ischemic stroke. *N. Engl. J. Med.* **2001**, *345*, 1444–1451. [CrossRef]
125. Hart, R.G.; Sharma, M.; Mundl, H.; Kasner, S.E.; Bangdiwala, S.I.; Berkowitz, S.D.; Swaminathan, B.; Lavados, P.; Wang, Y.; Wang, Y.; et al. Rivaroxaban for stroke prevention after embolic stroke of undetermined source. *N. Engl. J. Med.* **2018**, *378*, 2191–2201. [CrossRef] [PubMed]
126. Eikelboom, J.W.; Connolly, S.J.; Bosch, J.; Dagenais, G.R.; Hart, R.G.; Shestakovska, O.; Diaz, R.; Alings, M.; Lonn, E.M.; Anand, S.S.; et al. Rivaroxaban with or without aspirin in stable cardiovascular disease. *N. Engl. J. Med.* **2017**, *377*, 1319–1330. [CrossRef] [PubMed]
127. Morris, J.G.; Singh, S.; Fisher, M. Testing for inherited thrombophilias in arterial stroke: Can it cause more harm than good? *Stroke* **2010**, *41*, 2985–2990. [CrossRef] [PubMed]
128. Borissoff, J.I.; Spronk, H.M.; Heeneman, S.; ten Cate, H. Is thrombin a key player in the "coagulation-atherogenesis" maze? *Cardiovasc. Res.* **2009**, *82*, 392–403. [CrossRef] [PubMed]
129. Martorell, L.; Martinez-Gonzalez, J.; Rodriguez, C.; Gentile, M.; Calvayrac, O.; Badimon, L. Thrombin and protease-activated receptors (PARs) in atherothrombosis. *Thromb. Haemost.* **2008**, *99*, 305–315. [CrossRef]
130. Davis, M.J.; Menon, B.K.; Baghirzada, L.B.; Campos-Herrera, C.R.; Goyal, M.; Hill, M.D.; Archer, D.P.; Program, T.C.S. Anesthetic management and outcome in patients during endovascular therapy for acute stroke. *Anesthesiology* **2012**, *116*, 396–405. [CrossRef] [PubMed]
131. Takahashi, C.; Liang, C.W.; Liebeskind, D.S.; Hinman, J.D. To tube or not to tube? the role of intubation during stroke thrombectomy. *Front. Neurol.* **2014**, *5*, 170. [CrossRef] [PubMed]
132. Farag, E.; Argalious, M.; Toth, G. Stroke thrombectomy perioperative anesthetic and hemodynamic management. *J. Neurointerv. Surg.* **2023**, *15*, 483–487. [CrossRef] [PubMed]
133. Flottmann, F.; Leischner, H.; Broocks, G.; Faizy, T.; Aigner, A.; Deb-Chatterji, M.; Thomalla, G.; Krauel, J.; Issleib, M.; Fiehler, J.; et al. Emergency Conversion to General Anesthesia Is a Tolerable Risk in Patients Undergoing Mechanical Thrombectomy. *AJNR Am. J. Neuroradiol.* **2020**, *41*, 122–127. [CrossRef]
134. Simonsen, C.Z.; Yoo, A.J.; Sørensen, L.H.; Juul, N.; Johnsen, S.P.; Andersen, G.; Rasmussen, M. Effect of general anesthe- sia and conscious sedation during endovascular therapy on infarct growth and clinical outcomes in acute ischemic stroke. *JAMA Neurol.* **2018**, *75*, 470–477. [CrossRef]
135. Schönenberger, S.; Uhlmann, L.; Hacke, W.; Schieber, S.; Mundiyanapurath, S.; Purrucker, J.C.; Nagel, S.; Klose, C.; Pfaff, J.; Bendszus, M.; et al. Effect of conscious sedation vs general anesthesia on early neurological improvement among patients with ischemic stroke undergoing endovascular thrombectomy: A randomized clinical trial. *JAMA* **2016**, *316*, 1986–1996. [CrossRef] [PubMed]
136. Sørensen, L.H.; Speiser, L.; Karabegovic, S.; Yoo, A.J.; Rasmussen, M.; Sørensen, K.E.; Simonsen, C.Z. Safety and quality of endovascular therapy under general anesthesia and conscious sedation are comparable: Results from the GOLIATH trial. *J. Neurointerv. Surg.* **2019**, *11*, 1070–1072. [CrossRef] [PubMed]

137. Maurice, A.; Eugène, F.; Ronzière, T.; Devys, J.-M.; Taylor, G.; Subileau, A.; Huet, O.; Gherbi, H.; Laffon, M.; Esvan, M.; et al. General Anesthesia versus Sedation, Both with Hemodynamic Control, during Intraarterial Treatment for Stroke: The GASS Randomized Trial. *Anesthesiology* **2022**, *136*, 567–576. [CrossRef] [PubMed]
138. Zhang, L.; Dinsmore, J.; Khan, U.; Leyon, J.; Ogungbemi, A.; Trippier, S.; Clarke, B.; Luong, C.; Campbell, R.; Clifton, A.; et al. General Anesthesia Versus Conscious Sedation for Mechanical Thrombectomy in Acute Anterior Circulation Ischemic Stroke. *Stroke Vasc. Interv. Neurol.* **2022**, *2*, e000130. [CrossRef]
139. Liang, F.; Wu, Y.; Wang, X.; Yan, L.; Zhang, S.; Jian, M.; Liu, H.; Wang, A.; Wang, F.; Han, R.; et al. General Anesthesia vs Conscious Sedation for Endovascular Treatment in Patients with Posterior Circulation Acute Ischemic Stroke: An Exploratory Randomized Clinical Trial. *JAMA Neurol.* **2023**, *80*, 64–72. [CrossRef]
140. Geraldini, F.; Diana, P.; Fregolent, D.; De Cassai, A.; Boscolo, A.; Pettenuzzo, T.; Sella, N.; Lupelli, I.; Navalesi, P.; Munari, M. General anesthesia or conscious sedation for thrombectomy in stroke patients: An updated systematic review and meta-analysis. *Can. J. Anaesth.* **2023**, *70*, 1167–1181. [CrossRef]
141. Zhao, J.; Tan, X.; Wu, X.; Li, J.; Wang, S.; Qu, R.; Chu, T.; Chen, Z.; Liu, J.; Wang, Z. The efficacy and safety of general anesthesia vs. conscious sedation for endovascular treatment in patients with acute ischemic stroke: A systematic review and meta-analysis. *Front. Neurol.* **2023**, *14*, 1291730. [CrossRef]
142. Campbell, D.; Butler, E.; Campbell, R.B.; Ho, J.; Barber, P.A. General Anesthesia Compared with Non-GA in Endovascular Thrombectomy for Ischemic Stroke: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Neurology* **2023**, *100*, e1655–e1663. [CrossRef] [PubMed]
143. Sheth, S.A.; Lee, S.; Warach, S.J.; Gralla, J.; Jahan, R.; Goyal, M.; Nogueira, R.G.; Zaidat, O.O.; Pereira, V.M.; Siddiqui, A.; et al. Sex differences in outcome after endovascular stroke therapy for acute ischemic stroke. *Stroke* **2019**, *50*, 2420–2427. [CrossRef]
144. Silva, Y.; Sánchez-Cirera, L.; Terceño, M.; Dorado, L.; Valls, A.; Martínez, M.; Abilleira, S.; Rubiera, M.; Quesada, H.; Llull, L.; et al. Sex and gender differences in acute stroke care: Metrics, access to treatment and outcome. A territorial analysis of the Stroke Code System of Catalonia. *Eur. Stroke J.* **2023**, *8*, 557–565. [CrossRef] [PubMed] [PubMed Central]
145. Wasilczuk, A.Z.; Rinehart, C.; Aggarwal, A.; Stone, M.E.; Mashour, G.A.; Avidan, M.S.; Kelz, M.B.; Proekt, A.; ReCCognition Study Group; Basner, M.; et al. Hormonal basis of sex differences in anesthetic sensitivity. *Proc. Natl. Acad. Sci. USA* **2024**, *121*, e2312913120. [CrossRef] [PubMed] [PubMed Central]
146. Braithwaite, H.E.; Payne, T.; Duce, N.; Lim, J.; McCulloch, T.; Loadsman, J.; Leslie, K.; Webster, A.C.; Gaskell, A.; Sanders, R.D. Impact of female sex on anaesthetic awareness, depth, and emergence: A systematic review and meta-analysis. *Br. J. Anaesth.* **2023**, *131*, 510–522. [CrossRef] [PubMed]