

The Role of ABCD3-I, ABCD3 and ABCD2 in Determining the Short-Term and Long-Term Prognoses of Patients with Acute Transient Ischemic Attack Referred to Emergency Room: A Systematic Review and Meta-Analysis

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Abstract--- Introduction and Objective: The estimated risk of the incidence of stroke following a transient ischemic attack (TIA) is 5-20% within the first hour and year following its incidence. Various methods such as the use of ABCD2, ABCD3-I, and ABCD3 criteria have been employed to predict and identify the high-risk cases of TIA. Contradictory results have been, however, reported about the advantage of each index for the prediction of stroke over the others. The present systematic review was designed in an attempt to obtain a precise estimation of the results of the studies on the role of 3 criteria, namely ABCD2, ABCD3-I and ABCD3 in determining the short-term and long-term prognoses of patients suffering from acute transient ischemic attacks.

Materials and Methods: The present study was conducted as a systematic review of all studies carried out from 2000 to 2021 on the role of three criteria in determining the short-term and long-term prognosis of patients with acute transient ischemic attack. The search strategy was identified and then the PubMed, Scopus, Ovid and Web of Science databases were searched to select the relevant articles.

Results: A total of 439 studies were reviewed for the relation of their titles, objectives and abstracts with the research topic, and 389 articles were thoroughly studied. Finally, 33 relevant studies were reviewed. The results of our study indicated that the ratio of integrated ABCD2 scores greater than 4 and smaller than 4 for 7 days after TIA in patients with recurrent strokes was 11% and 4%, respectively. The ratio of the integrated ABCD2 scores greater than and smaller than 4 for 30 days after TIA in patients with recurrent strokes was also 31% and 5%, respectively. The ratio of the integrated ABCD2 scores greater than and smaller than 4 for 90 days after TIA in patients with recurrent strokes was 8% and 3%. Three studies analyzed the ABCD3-I score after 90 days in TIA patients, and the ratio of the integrated ABCD3-I score greater than and smaller than 4 in patients with recurrent stroke was 11% and 5%, respectively.

Conclusion: The predictive power of the ABCD2 index for predicting a 30-day stroke in patients with an integrated score of greater than 4 and lower than 4 exceeded the other criteria, whereas the predictive power of the ABCD3-I index for predicting a 90-day stroke in stroke patients was slightly higher than ABCD2.

Keywords--- Short-term Prognosis, Long-term Prognosis, Transient Ischemic Attack, Stroke, ABCD2, ABCD3.

I. Introduction

Cerebrovascular diseases are the third major cause of mortality in developed countries after cardiovascular diseases and cancer. The overall prevalence of these diseases is approximately 800 per 100 thousand cases, and about 700 thousand strokes a year occur in the United States [1, 2]. These diseases are classified into two major categories, namely transient ischemic attacks (TIA) and ischemic strokes (Ischemic stroke). [3] A transient ischemic attack refers to a transient period of neurological malfunction resulting from the involvement of a certain area of the brain, spinal cord or retina without acute infarction. Based on this definition, despite the fact that the TIA symptoms usually last less than 1-2 hours, this duration cannot be a reliable indicator for making a distinction between TIA and stroke [4].

In 2009, the American Heart Association and the American Stroke Association defined transient ischemic attack as a neurological dysfunction transient attack caused by focal ischemia of the brain, spinal cord, or retina without acute infarction. TIA is, in point of fact, considered a neurological emergency, and its correct and early diagnosis is critically important as early interventions can considerably mitigate the risk of subsequent strokes in the future [5].

The annual risk of post-TIA ischemic attack is approximately 3-4% on average. Almost 15 million people round the globe suffer an acute attack on a yearly basis. Ischemic stroke is considered the fourth cause of mortality in the United States and the main cause of long-term disability in the world. About 15% of people referred with stroke have a reported history of TIA prior to its incidence [6,7]. The effective prevention of stroke in patients with a history of TIA reduces its incidence. Patients should be examined and treated urgently because the rapid treatment of ongoing ischemia can mitigate the scope of the neurological damage and disability [9-7].

The risk of post-TIA stroke has been explored in many studies but the factors associated with an increase in the risk of post-TIA stroke have not been fully identified. Due to the presence of various TIA differential diagnoses such as seizure, syncope and migraine, physicians have not still reached full agreement on the diagnosis of TIA. The physician treating the patient is in charge of making the final decision in this regard. This physician can be an emergency or internal medicine specialist or a family doctor [10, 11].

According to recent evidence, the risk of stroke after TIA is estimated at about 5% in the first 48 hours, 10% in the first month, and 20% in the first year. Due to this short-term risk, TIA is considered a medical emergency, especially in the high-risk group. Several methods including the ABCD2 (age-blood pressure-clinical manifestation-duration-diabetes mellitus) criteria have been used to identify and categorize high-risk TIA patients. These criteria include age, blood pressure, clinical symptoms, duration and diabetes mellitus. Patients can be classified into the low-risk and high-risk groups based on the resulting score [12-14].

Due to the high incidence of cerebrovascular diseases and their high mortality rates in developing and developed countries, various studies have been conducted on the risk of post-TIA stroke, but the factors associated with an increased risk of post-TIA stroke have not been fully identified yet. Moreover, since previous research resulted in different results with regard to 3 criteria namely ABCD2, ABCD3-I and ABCD3 in determining the prognosis of TIA patients referred to the emergency rooms, all studies conducted on this topic between 2000 and 2021 as well as articles published on the Web of Science, Medline, Scopus, Embase, Cochrane Library databases were reviewed in this systematic review to obtain an accurate estimate of the exact role of these 3 criteria in determining the short-term and long-term prognoses of patients suffering acute transient ischemic attacks.

II. Method and Materials

The document review and reference meta-analysis methods were utilized to conduct this study. The articles published on the Web of Science, Medline, Scopus, Embase, Cochrane Library databases from 2000 to 2021 were used.

A total of 439 studies related to TIA were retrieved by searching through the online databases. After removing 50 duplicates, 389 studies were obtained. Finally, a total of 33 studies were included after screening the summaries, abstracts and bodies of the articles. The final 32 studies included 24 prospective observational cohort studies, 6 retrospective studies, and 2 unspecified studies. The durations for the examination of patients following TIA were different as follows: within 7 days (17 studies), within 30 days (5 studies), and within 90 days (23 studies).

In most studies, TIA was diagnosed by an emergency physician, and in 23 studies it was initially diagnosed by an emergency physician followed by a neurologist.

First, a list of titles and abstracts of all the articles accessible in the aforementioned databases was created by the researcher and it was independently examined to determine and select the relevant titles. Afterward, the related articles were independently included in study process. Studies that were not part of the preliminary studies or reviews that were not relevant to our topic were excluded. Next, the articles were assessed against the Joanna Briggs Institute Reviewers, which is a standard and well-known international checklist for evaluating the quality of articles. This checklist consists of various sections assessing different aspects of methodology, including sampling methods, measuring variables, statistical analysis, adjustment of confounders, the validity and reliability of the research instruments, and the research objectives.

The total number of patients with the ABCD2 and ABCD3-I score and the ratio of patients in each of the ABCD2 and ABCD3-I categories with recurrent strokes within 7, 30, 90 days were calculated for each study. We also calculated the mixed risks of stroke for the ABCD2 and ABCD3-I score for days 7, 30, and 90 through univariate random-effects meta-analyses and the study internal variance modeled as a binomial. In this section, the weight of each study was first calculated based on the variances of each study and the fixed effects model as the inverted variance. Next, the weight of each study was calculated based on the resulting prevalence values using techniques that were integrated to determine the heterogeneity in and between the studies and the random effect method and then Dersiminian and Laird were calculated. The heterogeneity index was determined by performing the heterogeneity test on the studies using the Cochran QI2 tests. The effect size of the studies was calculated following confirmation of heterogeneity. Analyses were carried out in Stata 17.0.

III. Results

The ABCD2 score after 7 days in TIA patients was studied in 17 studies [12, 15-30]. The study population included 18134 individuals. The average age of the participants in this study was 67.60 years, and 54.6% of the patients were male (Table 1). Moreover, 12 studies were prospective and 3 were retrospective. In two studies, the study type was not exactly determined. As seen in Figure 2, the ratio of the integrated ABCD2 score greater than 4 in patients with recurrent stroke was 0.11 (ES=0.11, 95%CI: 0.09-0.13, $p<0.001$) and the heterogeneity index revealed the heterogeneity between the studies ($I^2=98.73\%$, $Q=1264.04$, $p<0.001$). The results of the Egger test also showed no publication bias ($p=0.67$).

Table 1: Details of the Studies Selected for the Meta-analysis

Author's name and study year	Age	Males percentage	Disease type	Index	Measurement duration	Study type
Andrew 2010	67.4	45.2	stroke	ABCD2	7	prospective
Chandratheva 2010	72.5	43.8	TIA	ABCD2	7	prospective
Tsivgoulis 2010	67	67	stroke	ABCD2	7	prospective
L.H.S 2014	67.8	40.1	stroke	ABCD2	7	prospective
Appelros 2014	72.8	52.8	TIA	ABCD2	7	prospective
Johansson 2014	71	64	TIA	ABCD2	7	prospective
Zhang 2020	56.02	62.6	TIA	ABCD2	7	prospective
Cancelli 2011	76.4	51	TIA	ABCD2	7	prospective
Asimos 2010	67.4	45.2	TIA	ABCD2	7	prospective
Stead 2011	74	67	TIA	ABCD2	7	prospective
Calvet 2009	62.4	62	TIA	ABCD2	7	prospective
Cucchiara 2009	62		TIA	ABCD2	7	prospective
Hock 2010	61	63.3	TIA	ABCD2	7	Retrospective
Yan Xi 2019			TIA	ABCD2	7	Retrospective
MarcoBonifati 2011	68.7	46.4	TIA	ABCD2	7	Retrospective
Purroy 2010	70.3	61.6	TIA	ABCD2	7	-----
eJohnston 2007	65	47	TIA	ABCD2	7	-----
L.H.S 2014	67.8	40.1	stroke	ABCD2	30	prospective
Ottaviani 2016	73	57.5	TIA	ABCD2	30	prospective
Zhang 2020	56.02	62.6	TIA	ABCD2	30	prospective
Hock 2010	61	63.3	TIA	ABCD2	30	Retrospective
MarcoBonifati 2011	68.7	46.4	TIA	ABCD2	30	Retrospective
Tsivgoulis 2010	67	67	stroke	ABCD2	90	prospective
Wasserman 2010	67	50.9	TIA	ABCD2	90	prospective
Al-Khaled 2010	74.1	53	stroke	ABCD2	90	prospective
L.H.S 2014	67.8	40.1	stroke	ABCD2	90	prospective
Appelros 2014	72.8	52.8	TIA	ABCD2	90	prospective
Guarino 2015	69	51	TIA	ABCD2	90	prospective
Knoflach 2016	71.9	55.7	TIA	ABCD2	90	prospective
Amarenco 2016	66.1	60.2	TIA	ABCD2	90	prospective
Song 2019	56.95	61.7	TIA	ABCD2	90	prospective
Ildstad 2019	71.5	56.7	TIA	ABCD2	90	prospective
Amarenco 2012	64	52	TIA	ABCD2	90	prospective
Wasserman 2010	67	50.9	TIA	ABCD2	90	prospective
Cancelli 2011	76.4	51	TIA	ABCD2	90	prospective
Song 2013		58.8	TIA	ABCD2	90	prospective
Stead 2011	74	67	TIA	ABCD2	90	prospective
Calvet 2009	62.4	62	TIA	ABCD2	90	prospective
Cucchiara 2009	62		TIA	ABCD2	90	prospective
Harrison 2010	67	43	TIA	ABCD2	90	Retrospective
Hock 2010	61	63.3	TIA	ABCD2	90	Retrospective
Dutta 2016	72.6	50.6	TIA	ABCD2	90	Retrospective
MarcoBonifati 2011	68.7	46.4	TIA	ABCD2	90	Retrospective

Purroy 2010	70.3	61.6	TIA	ABCD2	90	-----
eJohnston 2007	65	47	TIA	ABCD2	90	-----
Yang 2010	66.3	56	stroke	ABCD2	365	Retrospective
Johansson 2014	71	64	TIA	ABCD3	7	prospective
Knoflach 2016	71.9	55.7	TIA	ABCD3 I	90	prospective
Song 2019	56.95	61.7	TIA	ABCD3 I	90	prospective
Xie 2021	62	65.5	TIA	ABCD3 I	90	prospective

Figure 1 indicates that the ratio of integrated ABCD2 score smaller than 4 in patients with recurrent strokes was 0.04 (ES=0.04, 95% CI: 0.02-0.05, $p<0.001$) and the heterogeneity index is indicative of the heterogeneity between studies ($I^2=89.37\%$, $Q=131.73$, $p<0.001$). The Egger test also shows no publication bias ($p=0.85$).

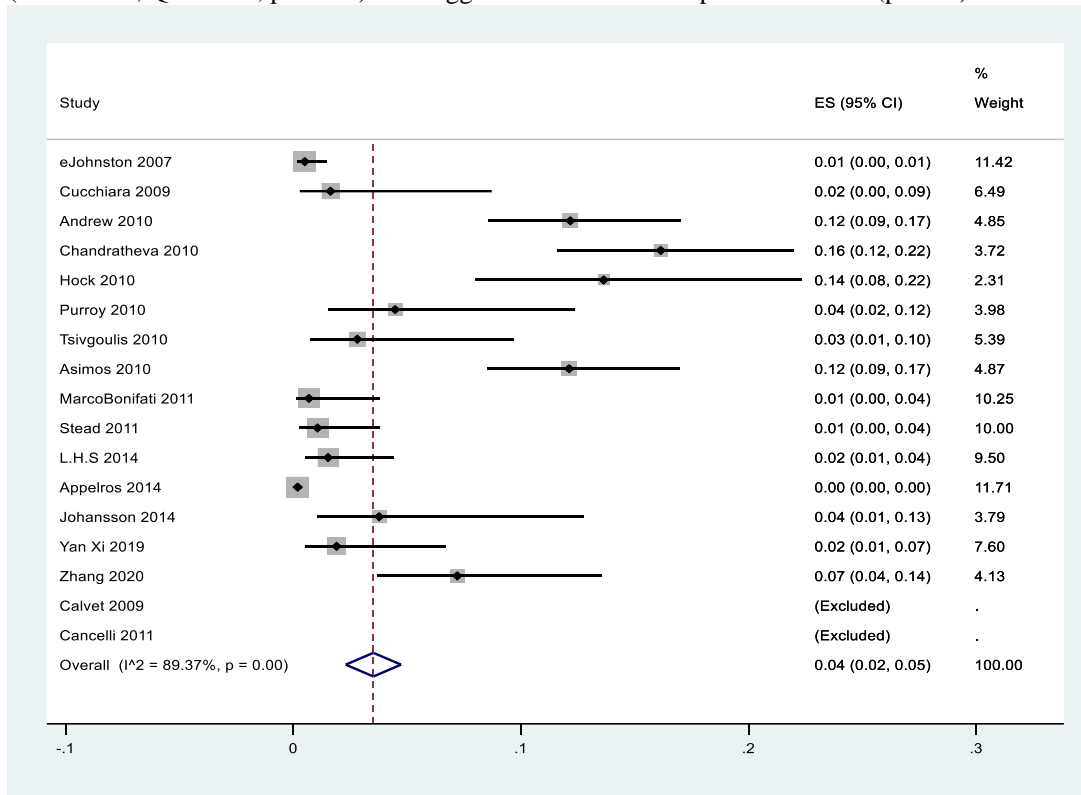


Figure 1: Analyzing the Role of ABCD2 Smaller than 4 in the 7-day Prognosis of TIA Patients

The ABCD2 score after 30 days in TIA patients was studied in five studies [23, 33-30]. The study population included 3880 participants. The average age of the participants was 65.30 years, and 53.98% of them were male. There were also 3 prospective studies and 2 retrospective studies. As shown in Figure 2, the ratio of integrated ABCD2 score greater than 4 in patients with recurrent strokes was 0.31 (ES=0.31, 95% CI: 0.16-0.45, $p<0.001$) and the heterogeneity index reflected the heterogeneity between the studies ($I^2=99.42\%$, $Q=688.90$, $p<0.001$). The Begg test also showed no publication bias ($p=0.10$).

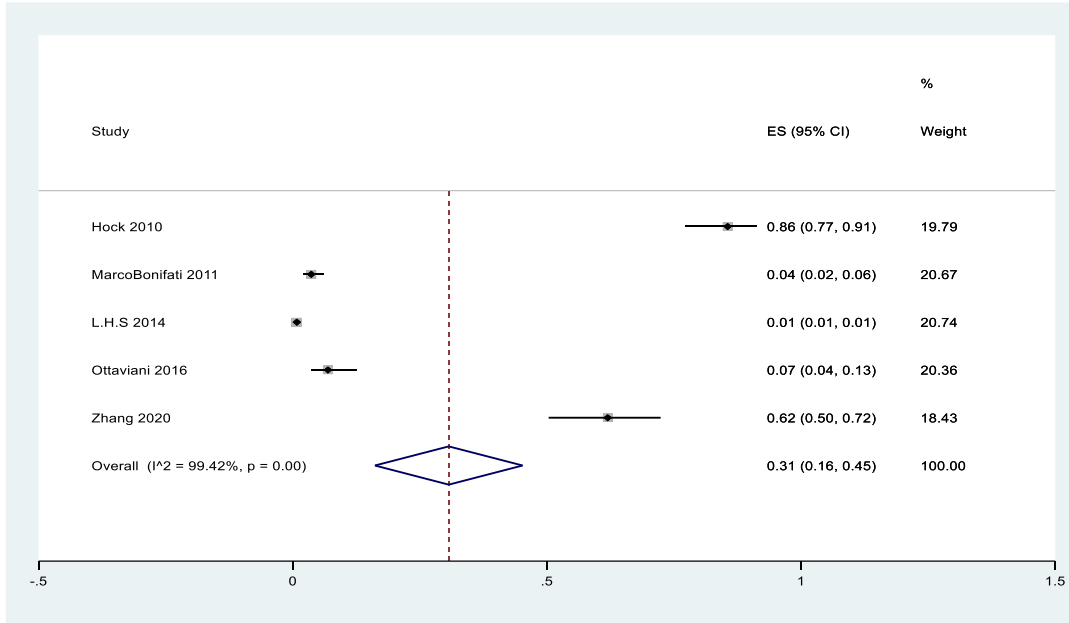


Figure 2: Analyzing the Role of ABCD2 Greater than 4 in the 30-day Prognosis of TIA Patients

Figure 3 indicates that the ratio of integrated ABCD2 score smaller than 4 in patients with recurrent strokes was 0.05 (ES=0.05, 95% CI: 0.02-0.09, p<0.001) and the heterogeneity index showed the heterogeneity between the studies (I²=85.18%, Q=26.98, p<0.001). The results of the Begg test also showed no publication bias (p=0.11).

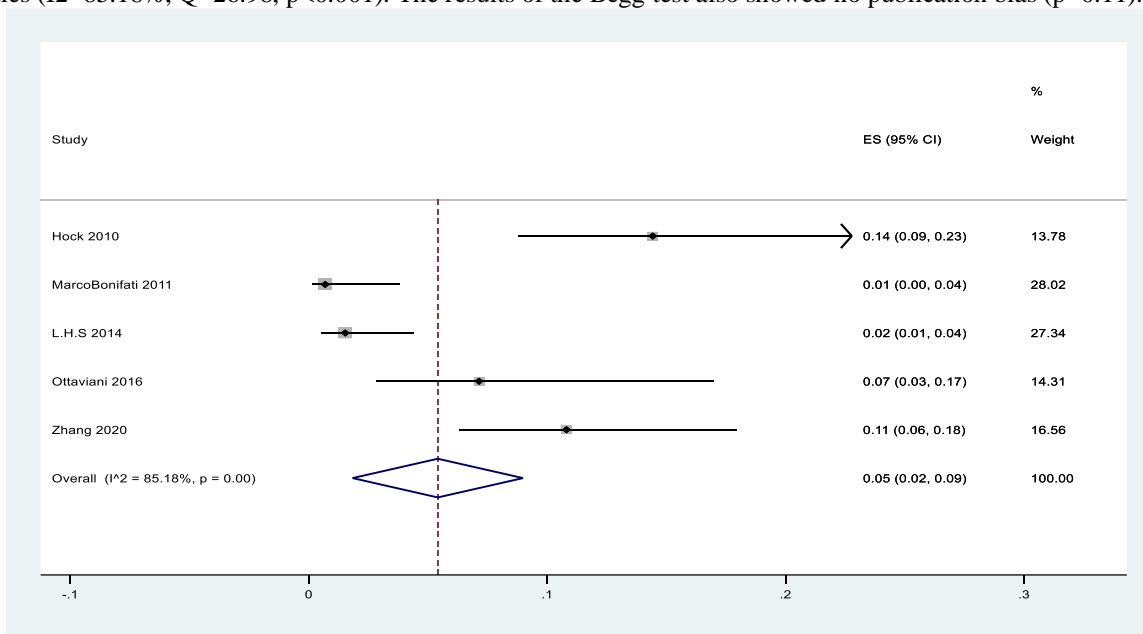


Figure 3: Analyzing the Role of ABCD2 less than 4 in the 30-day Prognosis of TIA Patients

The ABCD2 score after 90 days in TIA patients was analyzed in 22 studies [12, 16, 17, 19, 20, 26, 31-28, 44-33]. The study population included 23462 patients, the average age of the participants was 67.93 years, and 54.66% of the patients were male. Besides, 16 studies were prospective and 4 were retrospective, while in 2 studies the study type was not identified precisely. According to Figure 4, the ratio of the integrated ABCD2 score greater than 4 was 0.08 in patients with recurrent stroke (ES=0.08, 95% CI: 0.07-0.10), p<0.001) and the heterogeneity index was indicative of the heterogeneity between studies (I²=97.72%, Q=922.78, p<0.001). The Egger test results also showed no publication bias (p=0.32).

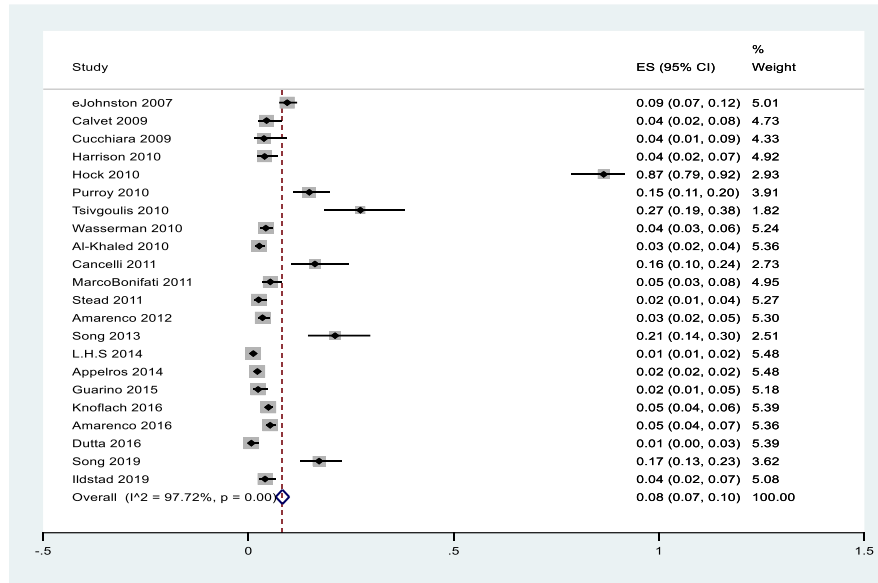


Figure 4: Analyzing the Role of ABCD2 Greater than 4 in the 90-day Prognosis of TIA Patients

As seen in Figure 5, the ratio of integrated ABCD2 score smaller than 4 in patients with recurrent stroke was 0.03 (ES=0.03, 95% CI: 0.02-0.03, $p < 0.001$) and the heterogeneity index showed the heterogeneity between the studies ($I^2=83.75%$, $Q=116.95$, $p < 0.001$). The Egger test also revealed no publication bias ($p=0.71$).

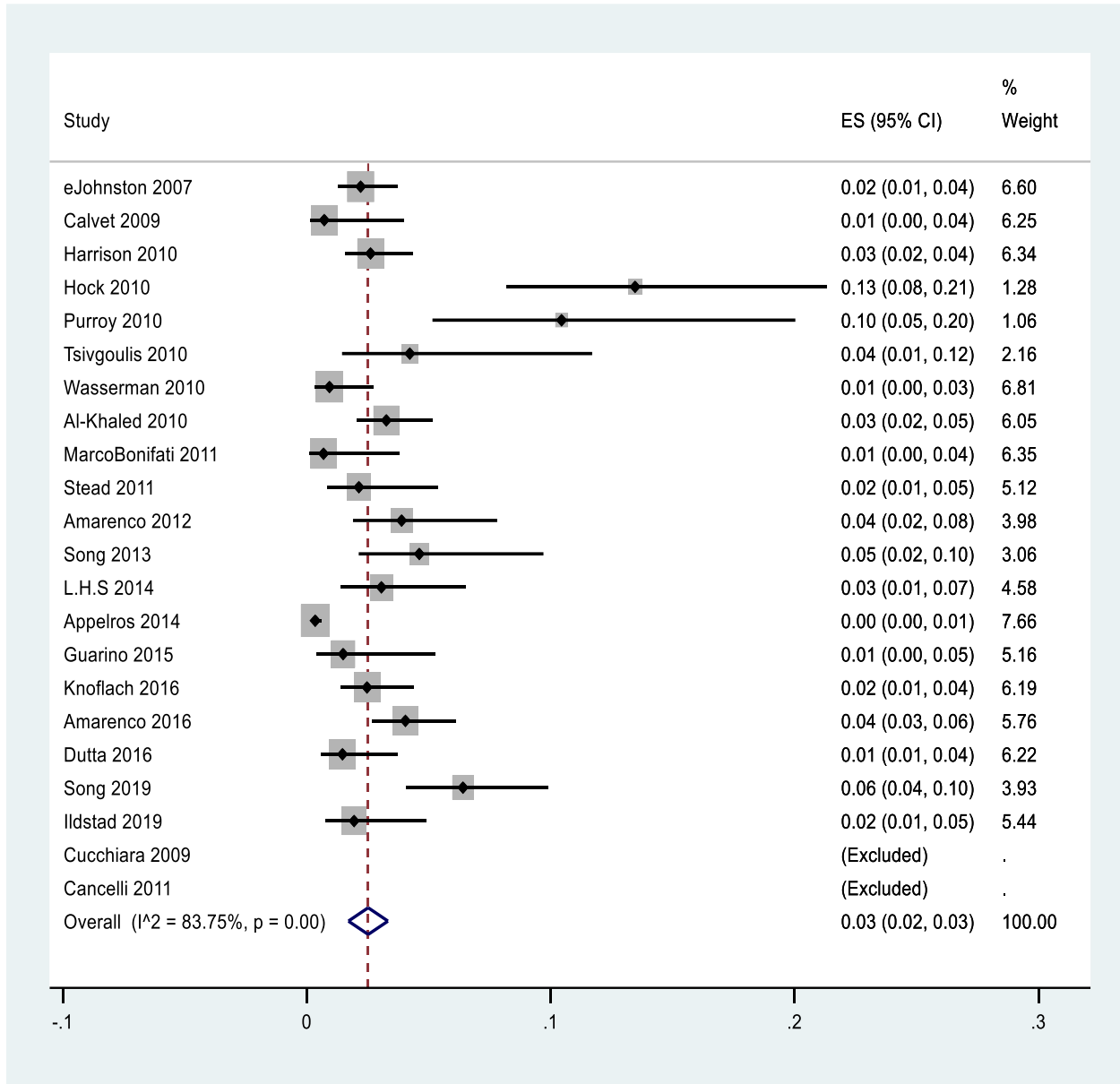


Figure 5: Analyzing the Role of ABCD2 Smaller than 4 in the 90-day Prognosis of TIA Patients

The ABCD3-I score after 90 days in TIA patients was studied in 3 studies [41, 43, 45]. The study population included 2558 patients. The average age of the participants was 62.63 years, and 60.97% of the patients were male. Moreover, 3 studies were prospective. Figure 6 indicates that the ratio of integrated ABCD3-I score greater than 4 in patients with recurrent stroke was 0.11 (ES=0.11, 95%CI: 0.03-0.19, p=0.01) and the heterogeneity index revealed the heterogeneity between the studies (I²=93.36%, Q=30.10, p<0.001). The Begg test also showed no publication bias (p=0.60).

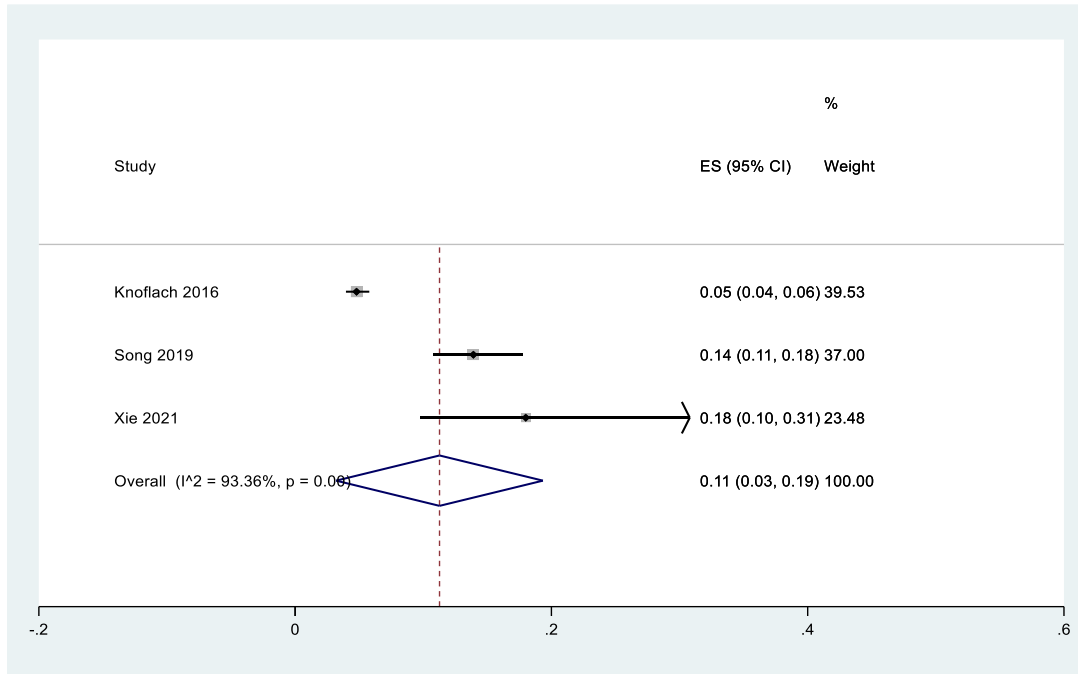


Figure 6: Analyzing the Role of ABCd3-I Greater than 4 in the 90-day Prognosis of TIA Patients

As shown in Figure 7, the ratio of the integrated ABCD3-I score smaller than 4 in patients with recurrent strokes was 0.05 (ES=0.02, 95%CI: 0.00-0.04, p<0.001), while the heterogeneity index showed the lack of heterogeneity between the studies (I²=44.81%, Q=3.62, p=0.016). The results of the Begg test also showed no publication bias (p=0.29).

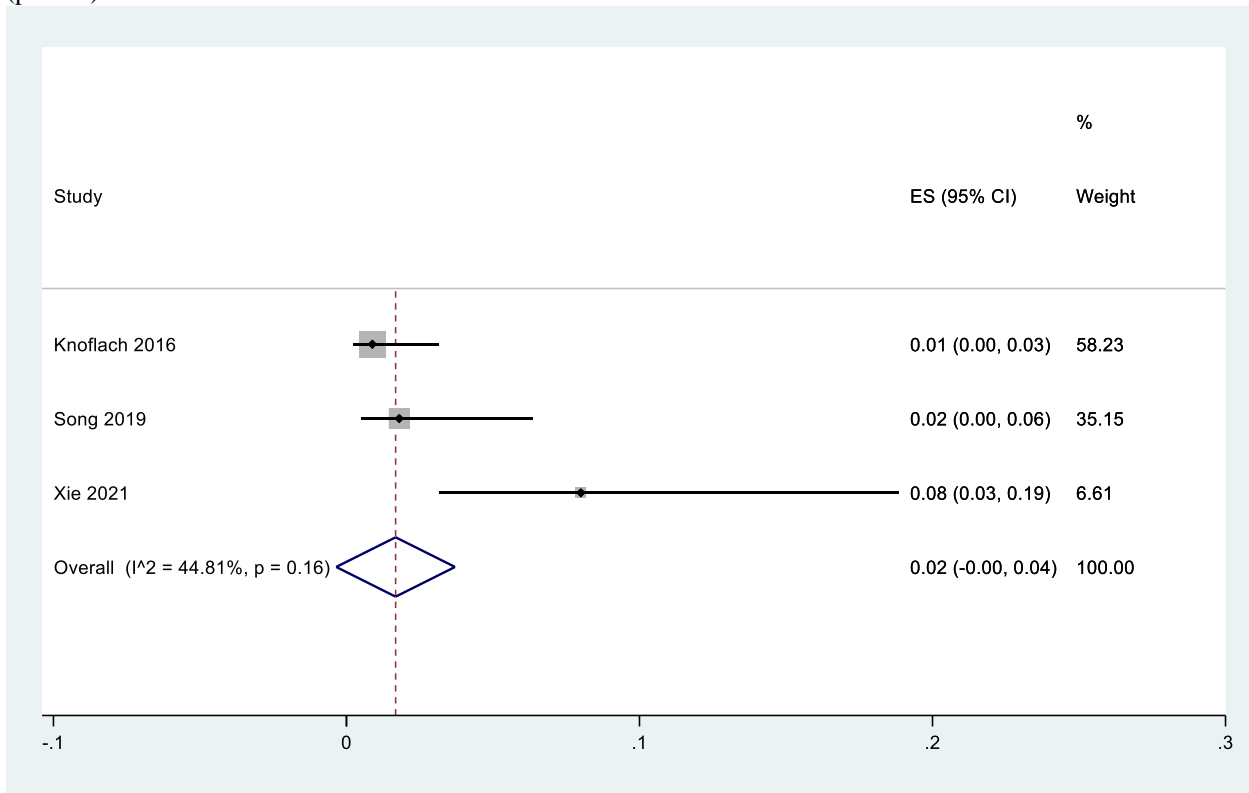


Figure 7: Analyzing the Role of ABCd3-I Smaller than 4 in the 90-day Prognosis of TIA Patients

IV. Discussion

Research results suggest that the estimated risk of the incidence of stroke after TIA is approximately 5% within the first 48 hours, 10% within the first month, and 20% within the first year. Various methods such as the use of ABCD2, ABCD3-I, and ABCD3 criteria have been employed to predict and identify the high-risk cases of TIA. Numerous studies have been carried out on the risk of incidence of stroke after TIA in the developing and developed countries, yet they have reported contradictory results regarding the advantage of each index for the prediction of stroke over the others. The present systematic review was designed in an attempt to obtain a precise estimation of the results of the studies on the role of 3 criteria, namely ABCD2, ABCD3-I and ABCD3 in determining the short-term and long-term prognoses of patients suffering from acute transient ischemic attacks. The results of our study generally suggest that the ratio of integrated ABCD2 score greater than 4 in patients with recurrent strokes was 11%, whereas the ratio of the integrated ABCD2 scores smaller than 4 in patients with recurrent strokes was 4%. The researchers in [23, 33-30] generally examined the ABCD2 score after 30 days in TIA patients, and their overall results revealed that the ratios of the integrated ABCD2 score greater than 4 and smaller than 4 in patients with recurrent strokes were 31% and 5%, respectively. Moreover, the ABCD2 score after 90 days in TIA patients was explored in 22 studies [12, 16, 17, 19, 20, 26, 31-28, 44-33], wherein the integrated results showed that the ratio of the integrated ABCD2 score greater than 4 and smaller than 4 in patients with recurrent strokes was 8% and 3%, respectively. In three studies [41, 43, 45], the ABCD3-I score after 90 days in TIA patients was examined, and the results showed that the ratio of the integrated ABCD3-I score greater than 4 and smaller than 4 in stroke patients was 11% and 5%, respectively. These ratios were 8% and 3% for the ABCD2 index after 90 days. The results of this study generally indicate that the predictive power of ABCD2 index for 30-day stroke was higher in patients with an integrated score of greater than 4 and smaller than 4 as compared to the other criteria. However, the predictive power of the ABCD3-I index for 90-day stroke in patients suffering from stroke was higher than ABCD2. The results of this study showed the ABCD2 index has had the highest use in different countries for the prediction of strokes, reflecting the significant role of this criterion in predicting strokes. Besides, in the present study, the role of all of the three ABCD2, ABCD3-I and ABCD3 indices in determining the short-term and long-term prognoses of patients with acute transient ischemic attack was inclusively assessed for the first time. The only weakness of this study was the small number of studies reported for short-term prognosis for the ABCD3 criterion.

According to the results of the present study and the collected data, which was acceptable and high quality data, the power of the ABCD2 index for predicting a 30-day stroke in patients with an integrated score of greater than 4 and lower than 4 exceeded the other criteria, whereas the predictive power of the ABCD3-I index for predicting a 90-day stroke in stroke patients was slightly higher than ABCD2. In other words, the ABCD2 criterion can provide more accurate estimates in the prediction of short-term prognoses up to 30 days, whereas the ABCD3-I criterion can provide more accurate estimates in the prediction of long-term prognosis.

V. Conclusion

According to the results of the present study and the collected data, which was acceptable and high quality data, the predictive power of the ABCD2 index for predicting a 30-day stroke in patients with an integrated score of greater than 4 and lower than 4 exceeded the other criteria, whereas the predictive power of the ABCD3-I index for predicting a 90-day stroke in stroke patients was slightly higher than ABCD2.

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VII. Conflict of Interest

Hereby, the authors declare that there is no conflict of interest regarding the present study.

VIII. Funding

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