

SPECIAL PAPER**Stroke in Southern Europe: A systematic review of the literature****Angelo V. Vasiliadis, PhD (c)****Laboratory of Adapted Physical Activity, Laboratory of Exercise Physiology and Biochemistry****Department of Physical Education and Sport Sciences at Serres, Greece****Medical Student, Medical School Aristotle University of Thessaloniki, Greece****Correspondence:** Angelo V. Vasiliadis, 3 Agias Sofias, 57010 Exochi, Thessaloniki

E-mail: vasiliadisvangelo@hotmail.com

Abstract

Background: Stroke is a leading cause of death and acquired disability worldwide. In Europe, strokes account for almost 1.1 million death per year. In particular, countries in Southern Europe constitute populations with a different lifestyle and dietary habits from those in Northern Europe and that may influence stroke incidence, type and risk factors.

Aim: The objective of this study was to review and summarise the trends of the incidence of stroke in Southern Europe, as well as, to mention stroke subtypes and recognise the risk factors for stroke.

Methods: A systematic review in PubMed was conducted.

Results: Therefore, twenty-three articles, representing seven countries, related to incidence, type and risk factors of stroke in this specific geographical area of Europe were identified. The annual stroke incidence varied from approximately 1.41 to 3.73 per 1000 population per year. Currently, in all the countries studied, ischemic stroke was the commonest stroke type in all series. Hypertension remains the main risk factor for both ischemic and hemorrhagic strokes, followed by diabetes mellitus, hyperlipidemia and other factors.

Conclusions: A wide range of stroke incidence may be due to the different lifestyle and behavioural factors among countries. Further research that uses the best possible methods to study the incidence, type and risk factors of stroke are urgently needed in Balkan Peninsula.

Keywords: epidemiology, stroke, incidence, Europe

Introduction

Stroke is a neurological disorder, a leading cause of death and a major acquired adult disability worldwide (Donnan et al., 2008). In Europe, stroke is the second most common cause of death, following ischemic heart disease (Álvarez-Sabín, 2008). Stroke by itself accounts for almost 1.1 million deaths per year in Europe, and at about one out of seven women (15%) and one out of ten men (10%) die from the disease (Nichols et al., 2012). Europe covers a great geographical area which is extended from the Arctic Ocean to the north, the Atlantic Ocean to the west and the Mediterranean Sea to the south. This regional differentiation of Europe's water borders contributes to climate variations across different part of the continent and also reflects to different geographic disparity in stroke incidence and mortality with northern countries in Europe

present a higher stroke incidence than those in the south (Bejot et al., 2007).

Current knowledge of stroke epidemiology is concentrate in many parts worldwide, such as South Asia (Kulshreshtha et al., 2012), Arab nations (Benamer and Grosset, 2009), North and South America (Roger et al., 2011, Saposnik and Del Brutto, 2003) or European studies (Truelsen et al., 2006) with scarce review data have been concentrated in Southern Europe. Because of variations on epidemiological and clinical characteristics of stroke according to environmental, economics and sociocultural factors, the need of aware of the peculiarities of stroke on Southern Europe is of great importance in order to reduce the impact of this epidemiological situation. The present paper is the first report on stroke epidemiology in this division of Europe and makes an effort to summarize

estimates of incidence, subtypes and risk factors of stroke in various countries. Therefore, this will be an important key in order to develop public health prevention programmes that reduce the stroke burden in this region.

Methods

Studies on stroke epidemiology in European population were searched through PubMed, from January 1990 to December 2011 with the words “epidemiology”, “stroke”, “incidence”, “Europe”. All the titles and abstracts were scanned by the author in order to identify eligible studies. Then, the full paper of potential studies was reviewed for more detailed assessment. Additionally, papers were identified from reference lists of retrieved articles, which were not included in the initially PubMed database search.

The inclusion criteria during this study were as follows: (i) Geographically, Southern Europe is the southern half of the landmass of Europe and according to the United Nations Statistics Division is composed of 16 member countries (Albania, Andorra, Bosnia and Herzegovina, Croatia, Gibraltar, Greece, Holy See, Italy, Malta, Montenegro, Portugal, San Marino, Serbia, Slovenia, Spain, FYROM) (Figure 1); (ii) Stroke was defined according to the World Health Organization (WHO Monica Project, 1998-1999); (iii) The study contained data about incidence, stroke types and risk factors; (iv) The study was published between January 1990 to December 2011, and written in English. After the search inclusions and exclusions, 23 epidemiological studies were eligible for the systematic review (Figure 2).

Results

Twenty-three population-based stroke studies that met the eligibility inclusion criteria were identified and included among the following European countries: Bosnia and Herzegovina (n=1) (Salinovic et al., 2009), Croatia (n=4) (Aleksic-Shihabi, 2010; Ivankovic et al., 2011; Lovrencic-Huzjan et al., 2006; Marjanovic et al., 2003), Greece (n=2) (Papadopoulos et al., 2006; Vemmos et al., 1999), Italy (n=12) (Carolei et al., 2002; Carolei et al., 1997; D'Alessandro et al., 2000; D'Alessandro et al., 1992; Di Carlo et al., 2003; Intiso et al., 2003; Lauria et al., 1995;

Manobianca et al., 2010; Manobianca et al., 2008; Musolino et al., 2005; Ricci et al., 1991; Rocca et al., 1998), Portugal (n=1) (Correia et al., 2004), Serbia (n=2) (Milojevic et al., 2011; Milosevic et al., 2010) and Spain (n=1) (Vega et al., 2009). In the past 2 decades, only 23 population-based or hospital-based studies from 7 countries were available for further analysis. The year of publication ranged from 1991 to 2011 (Table 1 & Figure 1).

Incidence

Only three from the above reported studies did not report stroke incidence. The incidence rate varied from 1.41 per 1000 population per year in Spain (Vega et al., 2009) to 3.73 per 1000 population per year in Croatia (Aleksic-Shihabi et al., 2010). There are ten studies from Italy which a reported stroke incidence rates ranged between 1.54 to 2.89 per 1000 population per year (Musolino et al., 2005; D'Alessandro et al., 2000). Also, the incidence of stroke in Spain based on three heterogeneous population groups and reflected significant variations. Castilla y Leon presented the highest incidence rate with 1.67 per 1000 inhabitants, whereas in Extremadura and Comunitant Valenciana it was 0.93 and 1.29, respectively (Vega et al., 2009). The main methodological characteristics and findings of the incidence of each country study are summarized in Table 1.

Gender and age

The repartition of the stroke sample according to gender is shown that the majority of studies (13 studies) found stroke more commonly in females than males and ranged from 50.5% to 62.1% for females (Salihovic et al., 2009; Aleksic-Shihabi, 2010; Ivankovic et al., 2011; Lovrencic-Huajzan et al., 2006; Carolei et al., 1997; D'Alessandro et al., 2000; D'Alessandro et al., 1992; Intiso et al., 2003; Lauria et al., 1995; Musolino et al., 2005; Ricci et al., 1991; Rocca et al., 1998; Correia et al., 2004). The data from Greece (Papadopoulos et al., 2006; Vemmos et al., 1999) appear to indicate that stroke is more common in male population, while two studies from Serbia and one study from Spain reported a slightly higher male preponderance at 50.7%, 50.6% and 51.9%, respectively (Milojevic et al., 2011; Milosevic et al., 2010; Vega et al., 2009).

Figure 1: Geographical region and composition of Southern Europe



Figure 2: Flow diagram shows a summary of the selected articles of the systematic literature review

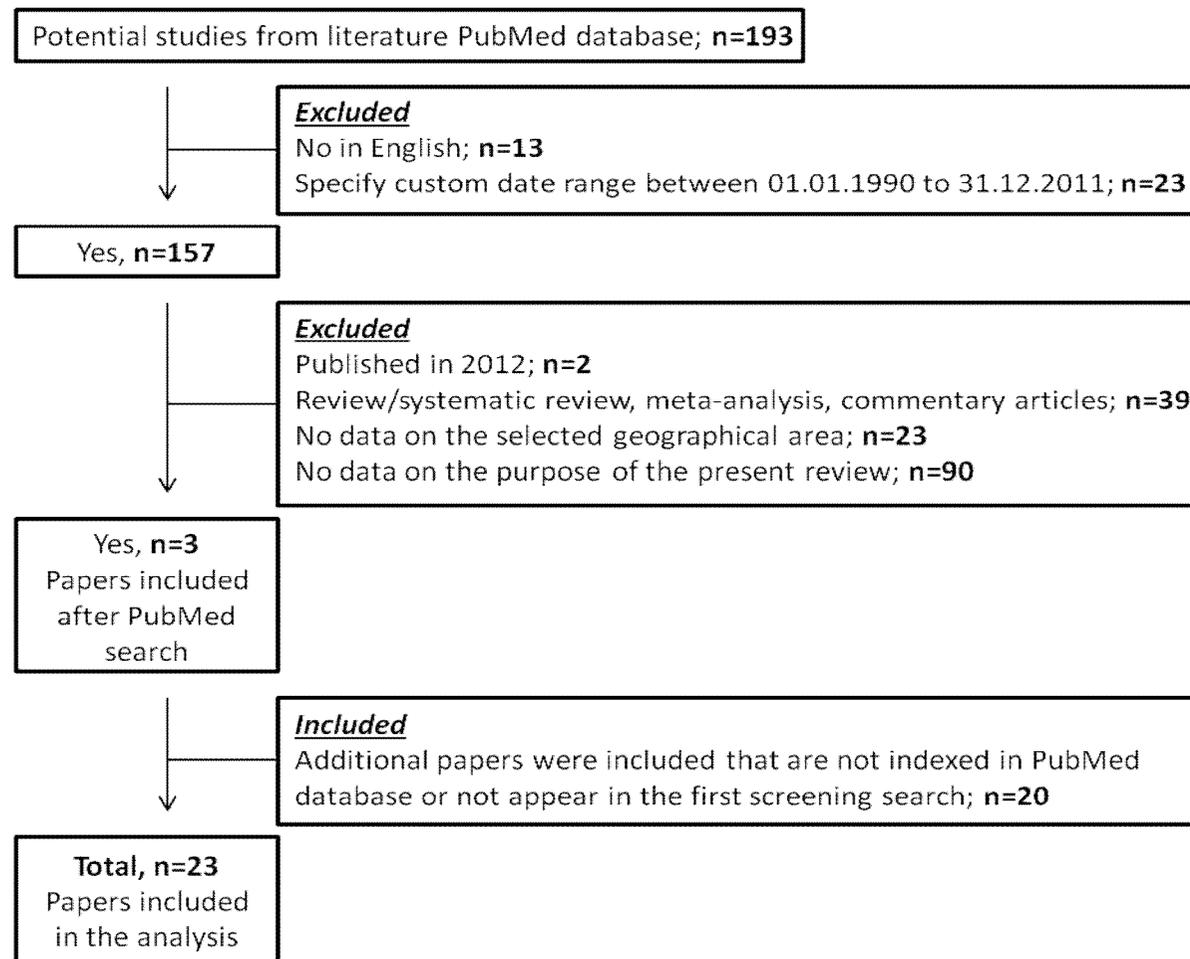


Table 1: Main characteristics and stroke estimates from population-based studies in Southern Europe

| Study | Country | Duration (years) | Study design | Event type | Age range | Mean age (years) | Sample | Male | Female | Incidence rates* |
|---------------------|-------------------------------|-------------------|---------------|-------------|-----------|---------------------|--------|-------|--------|---|
| Salihovic et al. | Bosnia and Herzegovina, | 2001-2005 (5) | Retrospective | First-ever | - | 65(m), 68(w) | 3864 | 47.1% | 52.9% | - |
| Aleksic-Shihabi | Croatia, Sibenik | 1996-2005 (10) | Retrospective | Not clear | - | 72.5('96),74.6('05) | 3819 | 48.5% | 51.5% | 2.77('96),3.73('05) |
| Ivankovic et al. | Croatia, Dubrovnik | 2008 (1) | Retrospective | Not clear | all | - | 247 | 44.9% | 55.1% | 1.8 |
| Lovrencic-Huajzan | Croatia, Zagreb | 1990 (1) | - | First-ever‡ | - | 73.3 | 662 | 42.9% | 57.1% | 1.98 |
| | Croatia, Zagreb | 1999 (1) | - | First-ever‡ | - | 68.2 | 1284 | 43.1% | 56.9% | 3.49 |
| Marjanovic et al. | Croatia, Baranya | 1997-2001 (4) | Retrospective | First-ever‡ | aged ≥ 25 | 68.4 | 211 | 51.7% | 48.3% | 1.6 |
| Papadopoulos et al | Greece, Xanthi | 1998-2002 (4) | Prospective | First-ever | - | 70.1 | 530 | 52.1% | 47.9% | 1.99 |
| Vemmos et al. | Greece, Arcadia | 1993-1995 (2) | Prospective | First-ever | aged > 18 | 75(m), 76(w) | 555 | 55.7% | 44.3% | 3.67 |
| Carolei et al.≡ | Italy, L'Aquila | 1994 (1) | Prospective | First-ever | aged > 18 | 74.8 | 819 | 48.6% | 51.4% | 2.75 |
| D'Alessandro et al. | Italy, Valley d'Aosta | 1996-1997 (1) | Prospective | First-ever | all | - | 343 | 47.2% | 52.8% | 2.89 |
| D'Alesandro et al. | Italy, Valley d'Aosta | 1989 (1) | Prospective | First-ever | aged > 18 | - | 254 | 44.1% | 55.9% | 2.23 |
| Di Carlo et al. | Italy, Vibo Valentia | 1996 (1) | Prospective | First-ever | aged > 18 | 71.9(m) , 74.2(w) | 321 | 51.1% | 48.9% | 1.79 |
| Intiso et al. | Italy, Foggia | 1993-1995 (3) | Retrospective | First-ever | all | 75 | 202 | 49.5% | 50.5% | 1.6 [#] ,1.67 ^{##} ,1.62 ^{###} |
| Lauria et al. | Italy, Belluno | 1992-1993 (1) | Prospective | First-ever | aged > 18 | - | 474 | 42.8% | 57.2% | 2.24 |
| Manobianca et al.≡ | Italy, Puglia | 2001-2002 (2) | Prospective | First-ever | aged ≥ 13 | 72.5(m), 77.5(w) | 127 | 60.6% | 39.4% | 1.6 |
| Musolino et al. | S. Italy, Aeolian archipelago | 1999-2002 (3) | Prospective | First-ever | aged > 18 | 72.5 | 62 | 41.9% | 58.1% | 1.54 |
| Ricci et al. | Italy, Umbria | 1986-1989 (3) | Prospective | First-ever | all | - | 375 | 48.8% | 51.2% | 2.54 |
| Rocca et al. | Italy, Sicily | 1984-1987 (3) | Retrospective | First-ever | aged ≥ 40 | - | 138 | 44.2% | 55.8% | 1.9 |
| Correia et al. | Portugal (rural area) | 1998-2000 (2) | Prospective | First-ever | aged > 18 | 74 | 226 | 48.2% | 51.8% | 3.05 |
| | Portugal (urban area) | | | | all | 72 | 462 | 37.9% | 62.1% | 2.69 |
| Milojevic et al. | Serbia, Kragujevac | 2003,04,07-09 (5) | - | Not clear | all | 68.8 | 4700 | 50.7% | 49.3% | - |
| Milosevic et al. | Serbia, Nis | 1996-2007 (11) | - | Not clear | all | 67.4 | 9675 | 50.6% | 49.4% | - |
| Vega et al. | Spain (CYL, EXT, CVA) | 2005 (1) | - | First-ever† | aged > 14 | earlier in men | 285 | 51.9% | 48.1% | 1.41 (1.67,0.93,1.29) |

*Per 1000 population per year (95% CI); ≡Two studies from the same authors team were investigated; †First-ever and history of disease; ‡First-ever and recurrent; CYL: Castilla y Leon; EXT: Extremadura; CVA: Comunitat Valenciana; m: men; w: women; #Ferković V and Sinanović O, 2002; #: 1993; ##: 1994; ###: 1995.

Table 2: Proportion of stroke subtypes in Southern Europe

| Study | Country | CT or MRI rate (%) | Time of CT/MRI after stroke | Stroke type | | | |
|----------------------------------|-------------------------|--------------------|-----------------------------|-----------------|----------|---------|------------------|
| | | | | IS, lacunar (%) | PICH (%) | SAH (%) | Undetermined (%) |
| Salihovic et al. | Bosnia and Herzegovina | CT (93.4) | - | 73.3, 32.8 | 15.8 | 4.3 | 6.6 |
| Aleksic-Shihabi | Croatia, Sibenik | - | - | 89.5 | | 10.5 | - |
| Ivankovic et al. | Croatia, Dubrovnic | CT | - | 87.85 | | 12.15 | - |
| Lovrencic-Huajzan et al. | Croatia, Zagreb (1990) | CT | - | 82.9 | 14.7 | 2.4 | - |
| | Croatia, Zagreb (1999) | | | 80.2 | 17 | 2.8 | - |
| Marjanovic et al. | Croatia, Baranya (2003) | - | - | 83.4, 15.3 | 15.6 | 1 | - |
| Papadopoulos et al. | Greece, Xanthi | CT and MRI | first 24-48 hours | 86.6 | | 13.4 | - |
| Vemmos et al. | Greece, Arcadia | CT (81.8) | within 7 days | 80.5, 12.6 | 13.9 | 2.5 | 3 |
| Carolei et al. [≡] | Italy, L'Aquila | CT or MRI (89) | within 7 days | 80.2, 24 | 14.9 | 2.9 | 2 |
| D'Alessandro et al. [‡] | Italy, Valley d'Aosta | CT or MRI | - | 83 | 10.4 | 4 | 2.6 |
| D'Alesandro et al. | Italy, Valley d'Aosta | CT (81) | first 48-72 hours | 67 | 13 | 2,3 | 17.7 |
| Di Carlo et al. | Italy, Vibo Valentia | CT | within 30 days | 72.9 | 19.3 | 3.7 | 4.1 |
| Intiso et al. | Italy, Foggia | CT or MRI | - | 86.1 | | 13.9 | - |
| Lauria et al. | Italy, Belluno | CT (89.5) | within 30 days | 67.3 | 19.7 | 2.5 | 10.5 |
| Manobianca et al. [≡] | Italy, Puglia | CT or MRI (93.7) | within 28 days | 72.4 | 18.9 | 2.4 | 6.3 |
| Musolino et al. | S. Italy | CT (82.2) | - | 67.8 | 12.9 | 1.6 | 17.7 |
| Ricci et al. | Italy, Umbria | CT (69) | within 30 days | 76.2, 19.6 | 9.9 | 4 | 9.9 |
| Correia et al. | Portugal (rural area) | CT (96.9) | within 30 days | 77.9 | 14.6 | 2.7 | 4.9 |
| | Portugal (urban area) | | | 75.3 | 16.3 | 3.7 | 4.1 |
| Milojevic et al. | Serbia, Kragujevac | - | - | 87.87 | 8.98 | 3.15 | - |
| Milosevic et al. | Serbia, Nis | CT or MRI | first 48 hours | 71.8 | 16.2 | 4.5 | 7.5 |

CT: brain computed tomography; MRI: brain magnetic resonance imaging; IS: ischemic stroke; PICH: primary intracerebral hemorrhage; SAH: subarachnoid hemorrhage; ‡D'Alessandro et al., 2000; ≡Two studies from the same authors team were investigated.

Table 3: Proportion of risk factors for stroke in Southern Europe

| Study | Country | Risk factors | | | | | | | | | | | | | | |
|----------------------|---------------------------|--------------|------|------|------------------|------|------|-----|-------|------|------|---------|------|---------|------|-------|
| | | HTN | DM | HPLD | Cardiac diseases | | | | | TIA | PAD | Smoking | AA | Obesity | PI | Other |
| | | | | | CHD/IHD | AF | HF | VHD | Other | | | | | | | |
| Salihovic et al. | Bosnia and Herzegovina | 70 | 21 | 11 | 40 | 14 | - | - | - | - | - | 28 | 8 | - | - | - |
| Lovrencic-Huzjan et | Croatia, Zagreb (1990) | 65 | 54 | 42 | 34 | 30 | 56 | - | - | - | - | 26 | 30 | - | - | - |
| | Croatia, Zagreb (1999) | 87 | 57 | 46 | 32 | 33 | 54 | - | - | - | - | 25 | 27 | - | - | - |
| Marjanovic et al. | Croatia, Baranya | 85.8 | 27 | 43.6 | | 46 | | - | - | - | - | - | - | - | - | - |
| Papadopoulos et al. | Greece, Xanthi | OR | OR | - | - | OR | - | - | - | - | - | - | - | - | - | - |
| Vemmos et al. | Greece, Arcadia | 81.1 | 29.2 | - | 20.2 | 34.1 | - | - | - | 16.6 | - | 19.9 | - | - | - | - |
| Carolei et al.≡ | Italy, L'Aquila | OR | OR | OR | OR | OR | - | - | OR | - | OR | OR | OR | - | - | - |
| D'Alessandro et al.‡ | Italy, Valley d'Aosta | OR | OR | OR | OR | OR | - | - | - | OR | - | OR | OR | - | - | - |
| D'Alesandro et al. | Italy, Valley d'Aosta | 54 | 20 | - | 12 | 18 | 17 | 6 | - | 14 | - | 21 | 23 | - | - | - |
| Intiso et al. | Italy, Foggia | 46 | OR | - | OR | - | - | - | - | - | - | 3.4 | 8 | - | - | - |
| Lauria et al. | Italy, Belluno (ischemic) | 54 | 18 | 19.5 | 21 | 24 | - | 3 | - | 13 | 14 | 18 | 19 | - | - | 2.5 |
| | Italy, Bel. (hemorrhagic) | 39 | 12 | 15.5 | 12 | 7 | - | 1 | - | 6 | 4 | 25 | 14 | - | - | 3 |
| Musolino et al. | S. Italy | 62 | 26 | 16 | - | 12 | 29 | - | - | 6 | - | 20 | - | - | - | - |
| Milojevic et al. | Serbia, Kragujevac | 41.4 | 15.4 | - | - | - | 18.4 | - | - | - | - | - | - | - | - | OR |
| Vega et al. | Spain | 58.2 | 26 | 29.8 | 29.8 | - | - | - | - | - | 11.2 | 14.4 | 10.9 | 24.6 | 43.2 | 34 |

HTN: hypertension; DM: diabetes mellitus; HPLD: hyperlipidemia; CHD/IHD: coronary heart disease/ischemic heart disease; AF: atrial fibrillation; HF: heart failure; VHD: valvular heart disease; TIA: previous history of transient ischemic attack; PAD: peripheral arterial disease; AA: alcohol abuse; PI: physical inactivity; OR: only referred without percentages; ‡D'Alessandro et al., 2000; All the number represent percentages (%); ≡Two studies from the same authors team were investigated.

The studies showed a mean age at onset of a first ever stroke within the seventh and eighth decade varying from 67.4 to 75 years. Also, men were considerably, on average, 3 years younger than women when experienced their first episode of stroke event (Salihovic et al., 2009; Vemmos et al., 1999; Di Carlo et al., 2003; Manobianca et al., 2008; Vega et al., 2009). The rates of stroke incidence, as it was expected, increased steeply with each decade of age and peaked in the age group at 85 years and older in both gender (Vemmos et al., 1999; D'Alessandro et al., 2000; D'Alessandro et al., 1992; Lauria et al., 1995). Stroke in the elderly (≥ 75 years) constituted the majority of stroke victims and surprisingly, three studies from Greece, Italy and Spain presented percentages above 60% of all stroke reported population (Vemmos et al., 1999; Manobianca et al., 2008; Vega et al., 2009).

Type of stroke

Among the studies reviewed, 19 provided information on the primary type of stroke. The most common type of stroke was ischemic stroke ranging from 67% to 89.5% and with the most studies accounting above 80 percent, whereas intracerebral hemorrhage occurred in 8.98-19.7% and subarachnoid hemorrhage in 1-4.5%. Among patients with ischemic strokes, only 5 studies implied proportions for lacunar infarction which are varied between 12.6% to 32.8%. Also, thirteen studies did not report proportions of classified types of stroke because of neither a neuroimaging technique nor necropsy data were available. The stroke subtypes from different southern Europe countries are presented in Table 2.

Only three of all 19 studies did not mention the use on of each imaging technique in order stroke is classified into ischemic and hemorrhagic stroke. The majority of studies in order to produce the final clinical diagnosis of stroke and determine the stroke subtypes classification, a detailed patient history of symptoms, a neurological examination and/or a appropriate diagnostic test (cerebral angiography, computed tomography (CT), magnetic resonance imaging (MRI), lumbar puncture) was used. The onset time of diagnostic test performed within 30 days of symptoms, while in three studies CT and/or MRI scan performed in

the first 72 hours from the event (Papadopoulos et al., 2006; D'Alessandro et al., 1992; Milosevic et al., 2010).

Risk factors

The most frequent risk factor for stroke was hypertension from southern Europe countries, being present in 39-87% of reported stroke patients (Lovrencic-Huzjan et al., 2006; Lauria et al., 1995). Diabetes mellitus was present in 12-57% (Lovrencic-Huzjan et al., 2006; Lauria et al., 1995). Hyperlipidemia was reported in 11-46% (Lovrencic-Huzjan et al., 2006; Salihovic et al., 2009). Other risk factors were as follows: cardiac disease (CHD/IHD, atrial fibrillation, heart failure, valvular heart disease) in 1-56% (Lovrencic-Huzjan et al., 2006; Lauria et al., 1995), alcohol abuse in 8-30% (Salihovic et al., 2009; Lovrencic-Huzjan et al., 2006), smoking in 3.4-28% (Salihovic et al., 2009; Intiso et al., 2003), previous history of transient ischemic attack in 6-16.6% (Vemmos et al., 1999; Lauria et al., 1995; Musolino et al., 2005), peripheral arterial disease in 4-14% (Intiso et al., 2003; Lauria et al., 1995). Two equally important risk factors, physical inactivity and obesity, were reported from only one study which conducted in Spain and represented 43.2% and 24.6%, respectively (Vega et al., 2009). Proportions of risk factor data is summarized in Table 3.

The main risk factors for ischemic stroke were hypertension (42.1% to 54%), followed by atrial fibrillation (24%) and CHD (21%) (D'Alessandro et al., 1992; Intiso et al., 2003; Lauria et al., 1995). Also, hypertension (39%) was the major risk factor for hemorrhagic strokes followed by cigarette smoking (25%) and alcohol abuse (14%) (Lauria et al., 1995). In a Spanish study showed that dyslipidemia, diabetes mellitus, smoking and alcohol consumption were more frequent in middle age (<75 years), while obesity and physical inactivity were more frequent in elderly patients with stroke (Vega et al., 2009). In a study conducted in Bosnia and Herzegovina reported that hypertension, diabetes mellitus, heart diseases and atrial fibrillation were more frequent in women, whereas, smoking and alcohol abuse were more common among men (Salihovic et al., 2009).

Discussion

To the best of our knowledge, in the present study, a review of stroke studies was performed since 1990 to 2011 on incidence from Southern Europe, as it was divided by the United Nations region classification (UNSD, 2013). Incidence data were available from 18 studies in five countries. The majority of these studies based on observations in urban population, although, this study also presents incidence rates based on population from rural areas (Aleksic-Shihabi, 2010; Marjanovic et al., 2003; Vemmos et al., 1999; Intiso et al., 2003; Manobianca et al., 2008; Correia et al., 2004).

Most of stroke studies were from Italy with an absence of published studies in the most of the countries from Balkan Peninsula. As result, incidence rates in Southern Europe varied from 1.41 per 1000 population per year in Spain (Vega et al., 2009) to 3.73 per 1000 population per year in Croatia (Aleksic-Shihabi et al., 2010). More than half of the studies had a prospective design, while a retrospective nature presented in six studies, while four studies did not mention their design type.

Available data the present study indicates that the incidence of stroke is generally similar with studies from the rest countries of Europe (Truelsen et al., 2006) and higher than in countries from the other side of Mediterranean Sea (Benamer and Gosset, 2009). Also, incidence rates of stroke from Southern Europe are higher than those from South America (Saposnik and Del Brutto, 2003) and studies from India based on urban and/or rural population (Kulshreshtha et al., 2012). In contrast, studies from USA, Oceania and Africa provide incidence rates range from 1.22 to 1.93, 1.28 to 2.06, and 0.95 to 1.08 (Walker et al., 2010; Feigin et al., 2009) respectively.

Unsurprisingly, ischemic stroke is the predominant stroke subtype in Southern Europe similar to other regions of the world (Kulshreshtha et al., 2012; Walker et al., 2010; Saposnik and Del Brutto, 2003). The results of the present study imply that the proportion of ischemic strokes range between 67% to 89.5%, with the most studies accounting over 80%. Only three studies present a proportion of ischemic

stroke below 70 percent and this may be due to the high proportion of undetermined and ill-defined classification of stroke or the lack of availability of any neuroimaging technique and the absence of necropsy data (Musolino et al., 2005; Lauria et al., 1995; D'Alessandro et al., 1992). Also, the classification of ischemic stroke subtype shows some variation within the studies among Southern Europe. The proportion of lacunar infarction range from 12.6 to 32.8% (Salihovic et al., 2009; Vemmos et al., 1999) and are similar to other studies from Kuwait and Saudi Arabia (Abdul-Ghaffar et al., 1997; Al Rajeh et al., 1993). The high rate of lacunar infarction (32.8%) in one study from Bosnia and Herzegovina may be associated with severe clinical picture, including lacunar state, hypertension and/or diabetes mellitus. In support of this, a non-communicable risk factor survey followed the WHO MONICA protocol and the later recommendations of the European Health Risk Monitoring (EHRM) project in the Federation of Bosnia and Herzegovina found that among subjects with mild and severe hypertension, 72% and 43.3% were not in treatment, respectively (Vučina, 2012).

Risk of stroke and recurrent stroke is influenced by a number of factors including risk factors difficult to control (age, gender and family history) and medical risk factors (hypertension, diabetes mellitus, hyperlipidemia/dyslipidemia). Studies in Southern Europe suggest a similar risk factor profile as in other countries worldwide, with hypertension being the most frequent risk factor, followed by hyperlipidemia, diabetes mellitus, cardiac diseases and lifestyle stroke risk factors (smoking, alcohol abuse, physical inactivity) (Benamer and Grosset, 2009; Saposnik and Del Brutto, 2003; Banerjee et al., 2001; Hajat et al., 2001).

Hypertension is the most prevalent risk factor after the age of 70-80 years and therefore the most important established and modifiable classic vascular risk factor for stroke patients (Engstad et al., 2012), while, antihypertensive treatment the most effective strategy for preventing stroke (Ravenni et al., 2011). Cardiovascular diseases also induce the risk of stroke, which increased dramatically with age (Engstad et al., 2012). Prevention programs for stroke population are of

great importance. Stroke can substantially reduced by a healthy and active way of life, a healthy and balanced diet plan and with discontinuing the practice of inhaling a smoked substance. Both public and professional education will help to promote the awareness that the implementation of a healthy lifestyle and nutrition is related to the progress in reducing the burden of stroke (Galimanis et al., 2009).

In conclusion, this systematic review shows a somewhat wide spectrum of incidence of stroke in Southern Europe countries. Well-designed epidemiological studies in Southern Europe, especially in Balkan Peninsula, are needed to monitor stroke incidence and risk factors. Accurate knowledge of incidence and stroke risk factors from community-based studies is important to develop public health interventions that reduce the stroke burden in such regions. Available data suggest that stroke subtype and risk factors found in stroke patients in Southern Europe countries are generally similar to the rest of Europe.

References

- Abdul-Ghaffar NU., El-Sonbaty MR., El-Din Abdul-Baky MS., Marafie AA., Al-Said AM. (1997) Stroke in Kuwait: a three-year prospective study. *Neuroepidemiology* 16; 40-47.
- Aleksic-Shihabi A. (2010) Stroke patients treated at department of neurology, Sibenik-Knin County General Hospital, 1996-2005. *Acta Clinica Croatica* 49; 3-9.
- Al-Rajeh S., Awada A., Niazi G., Larbi E. (1993) Stroke in a Saudi Arabian National Guard community. Analysis of 500 consecutive cases from a population-based hospital. *Stroke* 24; 1635-1639.
- Álvarez-Sabín J. (2008) In-hospital mortality in stroke patients. *Revista Española Cardiología* 61; 1007-1009.
- Banerjee TK., Mukherjee CS., Sarkhel A. (2001) Stroke in the urban population in Calcutta – an epidemiological study. *Neuroepidemiology* 20; 201-207.
- Bejot Y., Benatru I., Rouaud O., et al. (2007) Epidemiology of stroke in Europe: geographic and environmental differences. *Journal of the Neurological Sciences* 262; 85-88.
- Benamer HTS., Grosset D. (2009) Stroke in Arab countries: A systematic literature review. *Journal of the Neurological Sciences* 284; 18-23.
- Carolei A., Sacco S., De Santis F. (2002) Epidemiology of stroke. *Clinical and Experimental Hypertension* 24(7-8); 479-483.
- Carolei A., Marini C., Di Napoli M., Di Gianfilippo G., Santalucia P., Baldassarre M., De Matteis G., Di Orio F. (1997) High stroke incidence in the prospective community-based L'Aquila Registry (1994-1998), first year's results. *Stroke* 28; 2500-2506.
- Correia M., Silva MR., Matos I., Magalhaes R., Castro Lopes J., Ferro JM., Silva C. (2004) Prospective community-based study of stroke in northern Portugal. Incidence and case fatality in rural and urban populations. *Stroke* 35; 2048-2053.
- D'Alessandro G., Bottacchi E., Di Giovanni M., Martinazzo C., Sironi L., Lia C., Carenini L., Corso G., Gerbaz V., Polillo C., Presenti Compagnoni M. (2000) Temporal trends of stroke in Valle d'Aosta, Italy. Incidence and 30-day fatality rates. *Neurological Sciences* 21; 13-18.
- D'Alessandro G., Di Giovanni M., Roveyaz L., Iannizzi L., Presenti Compagnoni M., Blanc S., Bottacchi E. (1992) Incidence and prognosis of stroke in the Valle d'Aosta, Italy. First-year results of a community-based study. *Stroke* 23; 1712-1715.
- Di Carlo A., Inzitari D., Galati F., Baldereschi M., Giunta G., Grillo G., Furchi A., Manno V., Naso F., Vecchio A., Consoli D. (2003) A prospective community-based study of stroke in Southern Italy: The Vibo Valentia Incidence of Stroke Study (VISS). *Cerebrovascular Diseases* 16; 410-417.
- Donnan GA., Fisher M., Macleod M., Davis SM. (2008) *Stroke. The Lancet* 371; 1612-1623.
- Engstad T., Torgersen Engstad T., Viitanen M., Ellkjaer H. (2012) Epidemiology of stroke in the elderly in the Nordic countries. Incidence, survival, prevalence and risk factors. *Norsk Epidemiologi* 22; 121-126
- Feigin VL., Lawes CM., Bennett DA., Barker-Collo SL., Parag V. (2009) Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. *Lancet Neurology* 8; 355-369.
- Galimanis A., Mono ML., Arnold M., Nedeltchev K., Mattle HP. (2009) Lifestyle and stroke risk: a review. *Current Opinion in Neurology* 22; 60-68.
- Hajat C., Dundas R., Stewart JA., Lawrence E., Rudd AG., Howard R., Wolf CDA. (2001) Cardiovascular risk factors and stroke subtypes: Different between ethnic groups. *Stroke* 32; 37-42.
- Intiso D., Stampatore P., Zarrelli MM., Guerra GL., Arpaia G., Simone P., Tonali P., Beghi E. (2003) Incidence of first-ever ischemic and hemorrhagic stroke in a well-defined community of southern

- Italy, 1993-1995. *European Journal of Neurology* 10; 559-565.
- Ivankovic M., Drobac M., Gverovic-Antunica A., Dermarin V. (2011) The incidence of stroke at department of neurology, Dubrovnik General Hospital in 2008. *Acta Clinica Croatica* 50; 509-512.
- Kulshreshtha A., Anderson LM., Goyal A., Keenan NL. (2012) Stroke in South Asia: A systematic review of epidemiologic literature from 1980 to 2010. *Neuroepidemiology* 38; 123-129.
- Lauria G., Gentile M., Fassetta G., Casetta I., Agnoli F., Andreotta G., Barp C., Caneve G., Cavallaro A., Cielo R., Mongillo D., Mosca M., Olivieri P. (1995) Incidence and prognosis of stroke in the Belluno Province, Italy. First-year results of a community-based study. *Stroke* 26; 1787-1793.
- Lovrencic-Huzjan A., Zavoreo I., Rundek T., Demarin V. (2006) The changing incidence of cerebrovascular disease in Zagreb over a ten-year period. *Acta Clinica Croatica* 45; 9-14.
- Manobianca G., Zoccolella S., Petruzzellis A., Miccoli A., Logroscino G. (2010) The incidence of major stroke subtypes in southern Italy: a population-based study. *European Journal of Neurology* 17; 1148-1155.
- Manobianca G., Zoccolella S., Petruzzellis A., Miccoli A., Logroscino G. (2008) Low incidence of stroke in southern Italy. A population-based study. *Stroke* 39; 2923-2928.
- Marjanovic K., Soldo-Butkovic S., Kralj M., Soldo I., Marjanovic M., Nives H., Gmajnic R., Glasnovic M., Timarac J. (2003) The incidence of stroke in Baranya County (East Croatia). *Collegium Antropologicum* 27; 547-554.
- Milojevic D., Gajic V., Smailagic J., Donovic N., Toncev G., Gajic S. (2011) Biometeorological phases influence on stroke morbidity. *Medicinski Glasnik* 8; 229-236.
- Milosevic V., Zivkovic M., Djuric S., Vasic V., Pekmezovic T. (2010) Weekly variation of hospital admissions for stroke in Nis (Serbia). *Clinical Neurology and Neurosurgery* 112; 485-489.
- Musolino R., La Spina P., Serra S., Postorino P., Calabro S., Savica R., Salemi G., Gallitto G. (2005) First-ever stroke incidence and 30-day case fatality in the Sicilian Aeolian Archipelago, Italy. *Stroke* 36; 2738-2741.
- Nichols M., Townsend N., Scarborough P, Rayner M. (2012) *European Cardiovascular Disease Statistics*, 2012 edition. European Heart Network and European Society of Cardiology. Available from URL:<http://www.bhf.org.uk/publications/view-publication.aspx?ps=1002098> (accessed 25 February 2013).
- Papadopoulos V., Tsakiridis K., Filippou DK., Aggelopoulos P., Nikiforidis D., Baltatzidis G. (2006) Comparison of stroke among Christians and Muslims in Thrace, Greece. *Rural and Remote Health* 6; 505.
- Ravenni R., Jabre JF., Casiglia E., Mazza A. (2011) Primary stroke prevention and hypertension treatment: Which is the first-line strategy? *Neurology International* 3; 45-49.
- Ricci S., Grazia Celani M., La Rosa F., Vitali R., Duca E., Ferraguzzi R., Paolotti M., Seppoloni D., Caputo N., Chiurulla C., Scaroni R., Signorini E. (1991) SEPIVAC: A community-based study of stroke incidence in Umbria, Italy. *Journal of Neurology Neurosurgery and Psychiatry* 54; 695-698.
- Rocca WA., Reggio A., Savettieri G., Salemi G., Patti F., Meneghini F., Grigoletto F., Morgante L., Di Perri R for the Sicilian Neuro-Epidemiologic Study (SNES) Group. (1998) Stroke incidence and survival in three Sicilian municipalities. *Italian Journal of Neurological Sciences* 19; 351-356.
- Roger VL., Go AS., Lloyd-Jones DM., Adams RJ., Berry JD., Brown TM., Carnethon MR., Dai S., de Simone G., Ford ES., Fox CS., Fullerton HJ., Gillespie C., Greenlund KJ., Hailpern SM., Heit JA., Ho PM., Howard VJ., Kissela BM., Kittner SJ., Lackland DT., Lichtman JH., Lisabeth LD., Makuc DM., Marcus GM., Marelli A., Matchar DB., McDermott MM., Meigs JB., Moy CS., Mozaffarian D., Mussolino ME., Nichol G., Paynter NP., Rosamond WD., Sorlie PD., Stafford RS., Turan TN., Turner MB., Wong ND., Wylie-Rosett J. (2011) Heart disease and Stroke statistics - 2011 update: A report from the American Heart Association. *Circulation* 123; e18-e209.
- Salihovic D.O, Smajlovic DM., Sinanovic OI. (2009) Reduction of stroke mortality in the Tuzla region, Bosnia and Herzegovina. *Neurosciences* 14; 230-233.
- Saposnik G., Del Brutto OH. (2003) Stroke in South America - A systematic review of incidence, prevalence and stroke subtypes. *Stroke* 34; 2103-2108.
- Truelsen T., Piechowski-Jozwiak B., Bonita R., Mathers C., Bogousslavsky J., Boysen G. (2006) Stroke incidence and prevalence in Europe: a review of available data. *European Journal of Neurology* 13; 581-598.
- United Nations Statistics Division (2013) Composition of macro geographical (continental) regions, geographical sub-regions, and selected economic and other groupings. Available from URL:

- <http://unstats.un.org/unsd/methods/m49/m49regin.htm> (accessed 9 March 2013)
- Vega T., Zurriaga O., Mauro Ramos J., Gil M., Alamo R., Lozano JE., Lopez A., Miralles MT., Vaca P., Alvarez Mdel M., on behalf of the group of research for the RECENT project (2009) Stroke in Spain: Epidemiologic incidence and patterns; A health sentinel network study. *Journal of Stroke and Cerebrovascular Diseases* 18; 11-16.
- Vemmos KN., Bots ML., Tsibouris PK., Zis VP., Grobbee DE., Stranjalis GS., Stamatelopoulos S. (1999) Stroke incidence and case fatality in Southern Greece - The Arcadia Stroke Registry. *Stroke* 30; 363-370.
- Vučina Z. (2012) Non-communicable disease factor survey, Federation of Bosnia and Herzegovina. Available from URL: <http://www.who.int/fctc/reporting/partyreports/bosherreport/en/index.html> (accessed 10 March 2013).
- Walker R., Whiting D., Unwin N., Mugusi F., Swai M., Aris E., Jusabani A., Kabadi G., Gray WK., Lewanga M., Alberti G. (2010) Stroke incidence in rural and urban Tanzania: a prospective, community-based study. *The Lancet Neurology* 9; 786-792.
- WHO MONICA Project. MONICA Manual (1998-1999). PartIV: Event Registration. Section 2: Stroke event registration data component. Available from URL: <http://www.ktl.fi/publications/monica/> (accessed 28 February 2013).