

# Trends of Spontaneous Intracerebral Hemorrhage in Florence District Along Fifteen Years: A Brief Report

Luca Masotti<sup>1, \*</sup>, Federico Moroni<sup>1</sup>, Vieri Vannucchi<sup>1</sup>, Guido Grossi<sup>1</sup>, Giancarlo Landini<sup>1</sup>, Filippo Cellai<sup>2</sup>, Stefano Spolveri<sup>3</sup>, Mauro Pratesi<sup>4</sup>, Anna Poggesi<sup>5</sup>, Domenico Inzitari<sup>5</sup>

<sup>1</sup>Internal Medicine, Santa Maria Nuova Hospital, Florence, Italy

<sup>2</sup>Department of Informatic and Health Technologies, ESTAR, Tuscany, Italy

<sup>3</sup>Internal Medicine, Borgo San Lorenzo Hospital, Florence, Italy

<sup>4</sup>Emergency Department, Santa Maria Nuova Hospital, Florence, Italy

<sup>5</sup>Neuroscience Section, NEUROFARBA Department, University of Florence, Florence, Italy

## Email address:

luca.masotti@tin.it (L. Masotti)

\*Corresponding author

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**Abstract:** Spontaneous intracerebral hemorrhage (ICH) represents the most feared stroke subtype. Real world epidemiological data about trends in incident cases and in-hospital mortality lack. Therefore we performed this study aimed to answer this concern. International Classification of Diseases, 9<sup>th</sup> revision, Clinical Modification (ICD-9<sup>th</sup> CM) database referred to patients discharged from six Hospitals of Florence district, Tuscany, Italy in a period fifteen years long (2001-2015) was analyzed. We searched for code 431 as primary or secondary diagnosis at hospital discharge. Overall, 7452 patients were discharged with ICH as primary or secondary diagnosis. Of them, 3695 (49.5%) were females and 4363 (59.1%) were 75-years old and over. Cases of ICH increased from 461 in 2001 to 568 in 2015. The greatest increase was observed in patients 75 years old and over (216 cases in 2001, 339 cases in 2015). Overall, 2273 patients died during hospital stay, in-hospital mortality being 30.5%. In-hospital mortality increased according to age, being 18% in under 65 years and 35.9% in 75-years old and over. In-hospital mortality decreased from 30.8% in 2001 to 25.1% in 2015. The decrease in in-hospital mortality was observed irrespective of age. In Florence district, cases of ICH increased over the years, especially in very old people, whereas in-hospital mortality decreased irrespective of age.

**Keywords:** Intracerebral Hemorrhage, Epidemiology, Mortality, Elderly

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## 1. Introduction

About one of four acute strokes are represented by spontaneous intracerebral hemorrhage (ICH). Due to highest acute mortality and severe neurological disability, ICH represents the most devastating stroke subtype [1], [2]. Over the last thirty years, 30-days mortality seems to be unchanged as it has been demonstrated in a meta-analysis of studies published between 1983 and 2006 [3]. Overall, incidence is 24.6 per 100 000 person-years (95% CI 19.7–30.7) [3]. Incidence increase steadily with age. People 85 years old and older has ten-fold greater incidence compared to people under

45 years [3]. Despite this background in population, observational clinical studies demonstrated that hospital burden of ICH could be increased. In United States, it was observed a 18% increase in hospital admissions for ICH along the period 1991-2001 [4]. Similar results were found in United Kingdom along the period 1981-2006 for patients 75-years old and older [5]. In Italy, 18.000-25.000 new cases of ICH occur each year, making incidence 30-45/100.000 inhabitants/year [6]. In 2009 in Tuscany, Italy, spontaneous ICH burdened for 0.52% of overall hospital admissions [7].

30-day mortality rate approaches 40%, whereas more than one half of patients is dead along the 12 months after ICH [2]. ICH-related in-hospital mortality seems unchanged over

the years [8]. Impressive, one half of deaths occur in the first 48 hours [2]. In Italy, 7-days, 30-days, one-year and ten-years mortality were found respectively 34.6%, 50.3%, 59%, 75.9% [5]. In 2009 in Tuscany, Italy, in-hospital mortality was 24.3% (range 13.6-35.2%) with an age-dependent increase [7]. In-hospital mortality for ICH burdened for about 5% of whole in-hospital mortality [7].

In acute phase, few specific treatments such anti-hypertensive drugs and reversal therapy in coagulopathy-associated ICH are available only for selected patients and their benefits are questionable [9], [10], [11]. Moreover, benefits of surgical approach can be reserved to a small percentage of patients [12].

Real world epidemiological data about trends in incident cases and in-hospital mortality lack. Therefore we performed this study aimed to answer this concern.

## 2. Materials and Methods

International Classification of Diseases, 9<sup>th</sup> revision, Clinical Modification (ICD-9<sup>th</sup> CM) database referred to

patients discharged from the six Hospitals of Florence district (Careggi Hospital, Santa Maria Nuova Hospital, San Giovanni di Dio Hospital, Santa Maria Annunziata Hospital, Figline Valdarno Hospital and Borgo San Lorenzo Hospital), Tuscany, Italy in the years 2001-2015 was retrospectively analyzed. We searched for code 431 as primary or secondary diagnosis at hospital discharge. Endpoints of the present research were the number of cases and the number of deaths occurred each year. In-hospital mortality was reported as percentage of diagnoses.

## 3. Results

Overall, 7452 patients were discharged with ICH as primary or secondary diagnosis in the analyzed period. Of them, 3695 (49.5%) were females. 4363 patients (59.1%) were 75-years old and over, whereas 1678 of patients (22.5%) were 65-75 years old and 1411 (18.4%) were under 65 years. Cases of ICH were 23% increased over the years, from 461 in 2001 to 568 in 2015 (Figure 1).

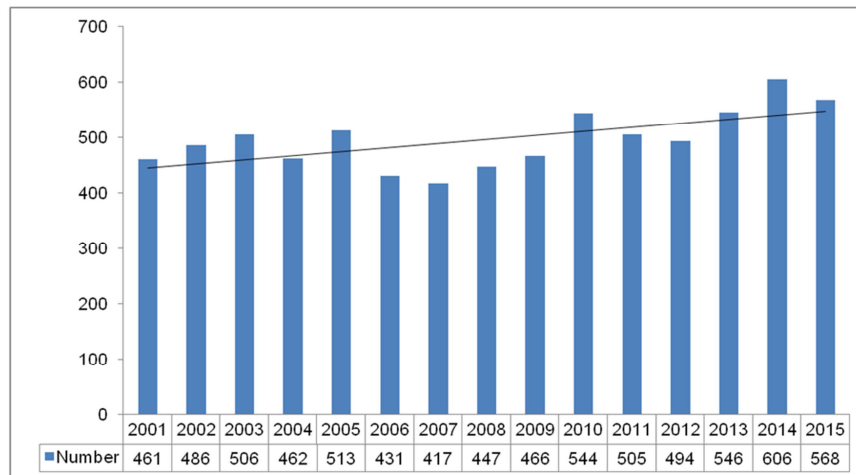


Figure 1. Trend in the cases of ICH in Florence district over the years 2001-2015.

The increase (57%) was observed only in patients 75 years old and over (216 cases in 2001, 339 cases in 2015), whereas in patients 65-75 years and under 65 years the increase was absent (Figure 2).

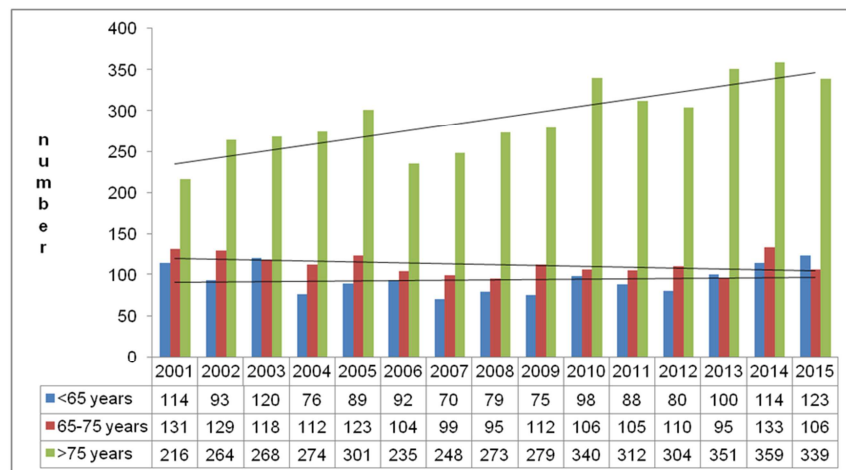
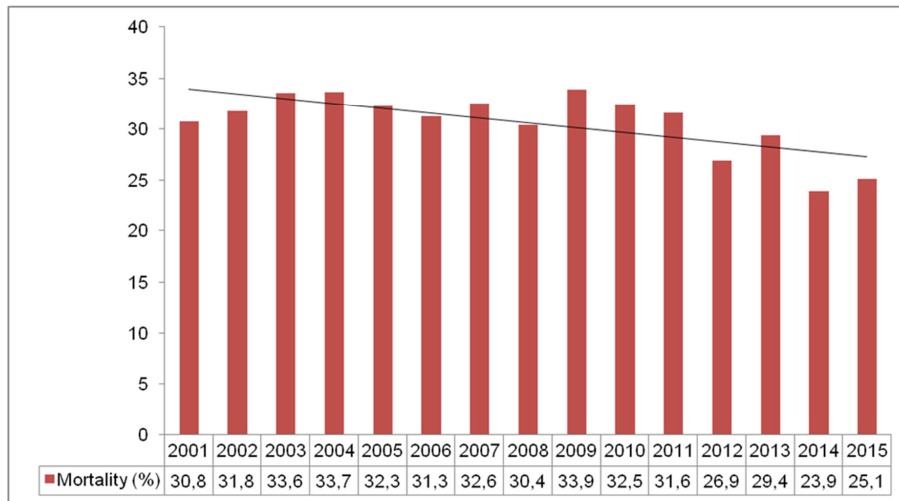


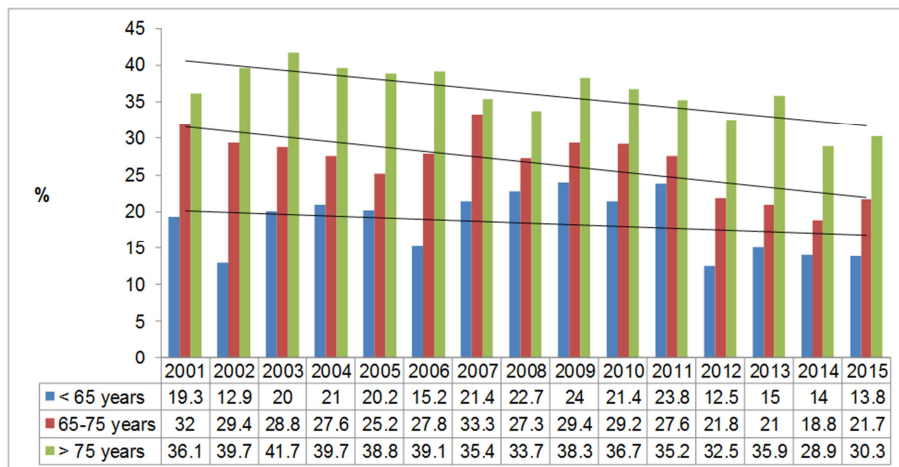
Figure 2. Trend in the cases of ICH according to age in Florence district over the years 2001-2015.

Overall, 2273 patients died during hospital stay, in-hospital mortality being 30.5%. Mean in-hospital mortality was 29.3% in males and 30.5% in females ( $p=ns$ ). In-hospital mortality increased according to age, being 18% in under 65 years patients, 26.2% in 65-75 years and 35.9% in 75-years old and over patients. In-hospital mortality decreased from 30.8% in 2001 to 25.1% in 2015 (Figure 3).



**Figure 3.** Trend in in-hospital mortality for ICH in Florence district over the years 2001-2015.

The decrease of in-hospital mortality was observed irrespective of age. The decrease in in-hospital mortality was about 6% in patients under 65 and over 75 years, whereas it was near 10% in patients 65-75 years old (Figure 4).



**Figure 4.** Trend in in-hospital mortality according to age in patients with ICH in Florence district over the years 2001-2015.

## 4. Discussion

Spontaneous ICH is a devastating illness and a worldwide healthcare problem, needing for a multidisciplinary approach from the Emergency Department arrival to the rehabilitation phase. Despite its pathogenesis, time course and clinical manifestations are well defined since many years, prognostic burden seems to be unchanged over the years, maybe because specific therapies are not available and interventional trials are failed leading to weak clinical practice recommendations [1], [2], [13], [14]. About one half of deaths occur in the first 48 hours, making the first hours as the golden hours also in ICH such as ischemic strokes.

However, steps forward have been made in the latest years

such as better prognostic stratification by using clinical practice grading scales or neuro-radiological findings (i.e. spot sign), the wider use of reversal strategies in coagulopathy related ICH, a better anti-hypertensive treatment, the allocation of appropriate settings (stroke units or neurointensive care), better global approach to complications such as dysphagia, infections or venous thromboembolism [13].

In the present study we analyzed trends in cases of spontaneous ICH diagnosed as primary or secondary discharge disease in patients admitted in all the Hospitals of Florence, one of the most populated towns of Italy with about one million inhabitants. We found that spontaneous ICHs increased over the years especially in very old patients. The increase in cases was about 20%, but it was about 50% in 75-

years old and older patients. To now, what may be the reasons for these trends are unclear. We postulate that aging population and the age-related diseases such as blood hypertension, atrial fibrillation and amyloid angiopathy and wider use of antithrombotic drugs such as vitamin K antagonists, direct oral anticoagulants and antiplatelets could explain the increased cases of ICH in patients 75-years old and over. In fact previous studies showed that anticoagulant-related ICHs increased over the years [5], [15], [16].

In our study we found that in-hospital mortality seems reduced, irrespective of age. The reduced mortality could be secondary to better global approach in acute phase. However, whether the reduced in-hospital mortality is masked by a reduced length of hospital stay remains unclear.

We recognize that our study has limitations, mainly due to the retrospective methodology. We used the ICD-9th CM, coding of which is operator depending. Therefore coding bias could be enclosed. Moreover, we enclosed only the patients who were admitted in Hospitals, therefore the number of cases and mortality could be underestimated due to lack of patients with ICH rapidly deteriorated and died in the setting of Emergency Departments, where compilation of hospital discharge schedules are not obligatory. Moreover the lack of a long term follow-up could underestimate the real burden of mortality. Therefore further prospective studies seem warranted to better clarify our results.

## 5. Conclusion

ICH is the most feared stroke subtype and efforts to reduce its burden should be encouraged. Epidemiological data are of utmost importance for planning an appropriate healthcare system. Our study demonstrates that in Florence district cases of ICH increased over the last fifteen years, especially in very old people, whereas in-hospital mortality decreased over the years. Prospective studies are warranted to better clarify our results.

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