Antonino D’Antona (1842-1913) was the first in describing the crush syndrome with renal failure following the Messina earthquake of December 28, 1908

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Abstract
There is confusion about the first description of the association between crush syndrome and renal failure. It has been traditionally attributed to Bywaters and Beall. The present study aims to analyze the problem by analyzing medical reports on the Messina-Reggio Calabria earth-quake of December 28, 1908 by using documents heretofore unknown. It demonstrates that first description of rhabdomyolysis with renal failure is attributed to Antonino D’Antona (1842-1913). D’Antona, professor of surgery at the University of Naples, coordinated the health net organized in Naples to assist persons wounded during the quake. Many of them in shock were transferred to Naples by ships. Franz von Colmers (1875-1960) was the chief surgeon of the German Mission of the Red Cross after the quake.
Because his late arrival, he did not treat patients with shock. He described rhabdomyolysis. The third medical report is that of Rocco Caminiti (1888-1946), collaborator of D’Antona at the University of Naples, and chief of surgery at the Loreto Hospital. He directed a rescue group in Villa San Giovanni and Reggio Calabria. In 1910, he reported on rhabdomyolysis in patients treated in the place of the disaster. Therefore the present study indicates that Antonino D’Antona holds the priority for description of rhabdomyolysis and kidney injury. There is no longer a place for the eponym Bywaters syndrome.

Key words: Antonino D’Antona, Franz von Colmers, rhabdomyolysis with renal failure, Rocco Caminiti

Introduction
The first description of Crush syndrome with renal failure is attributed to EGL Bywaters and D Beall because of their paper following the London Blitz [1], wherein the scientist did not acknowledge any predecessor. Following that paper the eponym Bywaters syndrome was generated. Historically the eponym is a mistake acknowledged even by Bywaters who was forced to admit the existence of predecessors in a letter to British Medical Journal [2].

That of Bywaters and Beall “was definitely a landmark paper, which focused attention on acute kidney injury and launched the subsequent cascade of studies that were to lead to the full emergence of acute renal failure during the ensuing decade”. [...] ”Bywaters and Beall rediscovered injury of the kidney in crush victims”[3].

However kidney injury following rhabdomyolysis has a longer history going back to the Messina Earthquake in 1908. Ori S. Better, an authority for crush syndrome, was appropriately distinguished for the studies at 1. traumatic rhabdomyolysis, 2. acute renal failure from war injuries and 3. the possible link between muscle damage and renal failure [1]. He pointed out that “traumatic muscle description was apparently first described in casualties of the 1909 Messina Earthquake by the German von Colmers [4]. Frankenthal in 1916 [5] was the first in describing traumatic rhabdomyolysis and acute renal failure resulting from war injuries [...] Minami in 1923 [6] described further cases of muscle crush injury and renal failure and raised the possibility that the muscle damage somehow contributed to the renal failure”. So it is evident that Better had not read the original paper of Franz von Colmers [7] and admitted that the source of that information was a paper of Bywaters published in 1990 [4].

Also recent papers from Vanholder et al and of Yoshioka et al [8] (full text) [9]. Vanholder and his associates pointed out that “In modern times the first cases of crush syndrome and ARF were reported during the Sicilian earthquake in Messina in 1908 and also in the German military medical literature during World war II. However they quote the paper on Bywaters and Beall of 1941 where such information is lacking [8] (full text). Also Yoshioka et al, [9] started their historical overview pointing out that “The first description of Crush Syndrome is considered to have appeared at the time of the Sicilian Earthquake”. However, they derived the information from the paper of Ori S. Better [1].

Aims
In order to understand who said it first in the field of rhabdomyolysis and or acute renal failure we have devised a study to analyze the pertinent literature related to people affected by the Earthquake-Tsunami of Messina and Reggio Calabria. The final goal was that of finding reports on rhabdomyolysis and or acute renal failure following that disaster which occurred on December 28, 1908 (magnitude 7.3 on the Richter scale).
Data will be provided indicating that there are 4 excellent scientific reports on the quake by scientists participating in rescue and health services. All of them described the crush of the muscle mass, but only 2 authored by Antonino D’Antona described rhabdomyolysis and renal failure.

Results
There were 4 exhaustive medical reports [7] [10] [11] [12]. Franz von Colmers on the activity of the Red Cross Hospital of the German Medical Expedition in Syracuse [7]. Rocco Caminiti’s [10] details on activity of his special rescue and care unit rescue of the special unit in Calabria. Antonino D’Antona and his associates reported on the activity of a special Earth Quake Hospital Net in Naples which started its activity on December 30, 1908, at 11.30 AM when the first hospital ship entered in the port of Naples.

Report of Franz von Colmers
Franz von Colmers was chief of the Hospital of the Red Cross during the German Mission to Syracuse. The unit reached Syracuse by train on January 12, 1909. The hospital, not in the frontline of the quake, took mainly care of patients already treated by local hospitals. It was operative immediately after arrival and ended its activity 48 days later, on February 28. The hospital took care of 119 persons, 83 of them were hospitalized for fractures, wounds, internal diseases due to the quake (mainly rheumatism) and minor surgeries. For each of them a narrative was reported and available for care. In the report (Figure 1) read to the German Society of Surgery in 1909 [7], v. Colmers referred to fractures, the gangrene due to compression (drückgangrene), the necrotic process of skin and muscles, and on the care and the healing of the wounds. There were 6 deaths. The hospital provided ambulatory care to some 300 patients. From the report, which was enriched by illustrations, emerges a good description of rhabdomyolysis. The kidney and the urinary tract are mentioned on 10 occasions. The reasons are highlighted in Table 1. He did not see patients with shock because of the time elapsed from the event (14 days).

Report of Rocco Caminiti
Rocco Caminiti was Chief of surgery at the Loreto Hospital in Naples and Clinical Professor of Surgery at the University of Naples (Figure 2). He was in his native town of Villa San Giovanni probably joining the family for Christmas and New Year 1909. His house was crushed, and he was personally slightly wounded. Caminiti immediately assembled a small and efficient rescue and care unit which was operative until January 28. He and his volunteers took care of 224 wounded persons (Figure 3), 11 of whom (4.5%) were in shock. His report is also special because of its accurate analysis of causes of death in the days immediately following the quake, gangrene being the main cause. “Gangrene was the most serious” [10].

“Muscle lesions were also very severe due to the fact that wounds were contusive in nature, or due to the compression under the debris or under beams for hours and days. Muscle substance was deprived of blood. This tissue, because of its fragility, was the most compromised. Blood vessels participated in the genesis of these primary and deep lesions, and their pathology favored and accelerated the lesions in other tissues and the subsequent gangrene” [10].
Concerning the lesions of internal organs he observed that “among them prevailed the lesions of the bladder, independently of the block of urine flow due to cross section of the spine”. There are many other reasons to read Caminiti’s report. Last but not least because it highlights the courage a surgeon has to generate when confronted with an insurmountable clinical disaster and lack of facilities at disposal, the hard times when even “bandaging was not sterile” [10].

In conclusion the report of Professor Caminiti, heretofore unknown, told how he took care of persons under the debris, some of them in shock, and also nicely described the crush syndrome. However he did not describe persons with kidney injury.

Report of Antonino D’Antona

The day after the quake (December 29) the Sicilian born Antonino D’Antona (Figure 4), professor of surgery and director of the division of surgery at the University of Naples, immediately enrolled a volunteer group of surgeons and nurses to work in his unit, and move directly to Messina. The group even reached the port to embark, but there was no ship available that evening. On the following day (December 30), in accordance with the Prefect of the city and of the Rector of the University, it was decided to organize a net of all Neapolitan Hospitals (29 in total), hospitals [11][12] to take care of the patients which were transferred by ship to Naples, the first one arrived at 11.30 AM that morning. D’Antona, because of his national and international reputation, was nominated chief of the net. The surgeons of the University Clinic were waiting for the patients on the dock. Private citizens put at their disposal private cars in order to move the patients into the various hospitals. A total of 1862 persons were hospitalized, of which 110 (5.9%) were in shock (Table 2).

D’Antona personally took care of 192 patients (the most critical), 7 of them were in shock (3.7%). The clinical status and the outcome of each of them was described [11][12]. There were 22 deaths (11.4%). Six out 7 patients in shock died (86.7%). Two patients died because of acute uremia. Patients nos. 116 and 120 [11][12], (Table 3).

D’Antona et al well described and discussed the pathogenesis crush syndrome (Figure 5, Figure 6, Figure 7). The “Pathogenetic event was for all

Table 2. The Neapolitan hospital net for patients directed by Antonino D’Antona. Compiled from data in references 12,13

<table>
<thead>
<tr>
<th>Causes</th>
<th>No.</th>
<th>Deads (No.)</th>
<th>Deads (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitals</td>
<td>29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contused</td>
<td>330</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scraped</td>
<td>330</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wounded</td>
<td>388</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Luxation, distortions</td>
<td>48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burned</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fractured</td>
<td>307</td>
<td>20</td>
<td>6.5</td>
</tr>
<tr>
<td>Shocked</td>
<td>110</td>
<td>61</td>
<td>5.5</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Neurological</td>
<td>73</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>- Infections</td>
<td>106</td>
<td>20</td>
<td>18.8</td>
</tr>
<tr>
<td>- Gangrene</td>
<td>138</td>
<td>37</td>
<td>26.8</td>
</tr>
<tr>
<td>- Tetanus</td>
<td>30</td>
<td>22</td>
<td>73.3</td>
</tr>
<tr>
<td>Total</td>
<td>1862</td>
<td>154</td>
<td></td>
</tr>
<tr>
<td>Improved/healed</td>
<td>1708</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deads</td>
<td>154</td>
<td>1862</td>
<td>(8.27%)</td>
</tr>
</tbody>
</table>

Table 3. Causes of death in 22 patients died at the division of surgery of the University of Naples (12,13)

<table>
<thead>
<tr>
<th>Causes</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock</td>
<td>6</td>
</tr>
<tr>
<td>Meningitis</td>
<td>1</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1</td>
</tr>
<tr>
<td>Bronchopneumonia</td>
<td>1</td>
</tr>
<tr>
<td>Cystitis</td>
<td>1</td>
</tr>
<tr>
<td>Gangrene</td>
<td>5</td>
</tr>
<tr>
<td>Tetanus</td>
<td>5</td>
</tr>
<tr>
<td>Nephritis</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
</tr>
</tbody>
</table>
persons a violent compression-transient or lasting hours and days”. Skin lesions presented “as black or pitch-black irregular spots with distinct borders which did neither protrude nor become hollow in relation to the intact skin, where they appeared as mounted. The contrast health and diseased skin was clear cut. These necrotic spots were leather hard to the touch, but definitely compressible. Surgeon scissors revealed the kind of lesions as well as their extension... However there were also translucent yellow, or amber-yellow- spots always well delimited over the whole skin”. There were “mechanical necrosis as well as anemic necrosis with venous thrombosis”. However “the area of the spots were not indicative to neither the extension nor of the depth of the lesions”. Concerning blood vessels, he pointed out that “small and large arteries may be not affected even when they are deep in a necrotic tissue” [11][12].

The data on the patients hospitalized in Naples were illustrated by Antonino D’Antona, Luigi Rizzo and Antonio Damascelli at the Congress of the Italian Society of Surgery on October 31, 1909, which took place in Rome. Of the 197 patients under his direct care at the University Surgical Clinic seven were in shock and two of them died of uremia.

Discussion
After the Messina earthquake four outstanding reports were published [7] [10] [11] [12], based on experience made on 2205 patients. Recognition for the reports on crush syndrome has been continuous for Colmers [1][2][3][4]. Caminiti was never quoted. Giuseppe Armocida quoted D’Antona in the entry of Encyclopedia Treccani [13]. Crush syndrome with renal failure was described by Antonino D’Antona [11][12], but it was never men-
tioned. Probably he wrote so many outstanding procedures that historians were never attracted by this primacy. Language difficulties may have played a role. However he had an international reputation and Spencer Watson of the great Northern Hospital in London came to Italy to assist his surgical sèances. After assisting at two surgeries by D’Antona in Naples, he wrote “his ability will be not overcome neither in Europe nor in United Sates” [14], however even his main biographer did not catch this novelty [14]. Bywaters had no primacy, no right to the eponym, although he was forced to admit that there were many other scientists who paved the way.

At the time of the earthquake of Messina and Reggio Calabria, little was known about shock. World War I stimulated interest in the topic. Many ad hoc committees were nominated in USA, United Kingdom, France and Germany. Outstanding scientists were attracted to such studies like W. M. Bayliss (General Physiology University College of London), A. N. Richards (University of Pennsylvania), and Walter B. Cannon (Harvard University). The latter published in 1923 an epochal monograph on Traumatic Shock which characterized pathogenesis, laboratory investigations and therapy [3][15].

From Cannon we learn that leukocytosis, starvation acidosis, increased non-urea non-protein nitrogen emerged as distinct markers. There was an increase of residual nitrogen (total non-protein nitrogen minus urea nitrogen) in non-catabolic cases as well as an increase of urea and non-urea blood nitrogen in the more catabolic patients which was related the low blood pressure. Urine was characterized by increased ammonia and acetoxy bodies. The toxic effects of nitrogenous substances liberated by the crush were suspected. It was established that it was important to correct body fluid either by forcing oral water intake, or by the intravenous route. Sodium bicarbonate had to be injected for acidosis. Infusion of plasma expanders was seen capable to restore low blood pressure permanently. The use of blood which was highly valuable however, was not superior to plasma expanders in pure shock. It was also learned that surgery was possible in shocked persons, with a low mortality for an operation performed in the early hours after the accident. Fluid resuscitation was a central step in management of patients with crush syndrome and fully adopted by Bywaters. This manoeuvre has been recently turned into a modern guideline [16].

Biographies of D’Antona, Colmers and Caminiti

Antonino D’Antona
He was born in Riesi, province Caltanissetta (Sicily) on December 18, 1842. High school studies were in Naples, Medical studies in Palermo (1860-1863) and Naples (1863-1865). At the age of 23, he received his MD in 1866. In the years 1866-1869 he trained in surgery in various European Universities: in Vienna with Theodor Billroth, in Leipzig with Karl Tiersch, in Berlin with Bernard Rudolf Conrad Langenbeck, in London with T. Spencer Wells and in Edinburgh with Joseph Lister. Subsequently he became in Naples a member of the university surgical team of Carlo Gallozzi and opened a private office where he taught surgery. In 1884 he was nominated surgeon at the Pilgrim Hospital in Naples where four years later he was additionally appointed pathologist (a very coveted position). In 1881 he won the national context for a professorship in surgery at the University of Padua, in 1884 that for professor of surgery at the University of Naples and in 1885 that at the University of Modena. He opted for Naples. He turned into a surgeon of unsurpassed skill, and opened many fields being excellent in abdominal, brain, and tuberculosis surgery. He mastered ovariectomy. He was particularly known for the nephrectomy using the extraperitoneal route. In 1896 he was nominated by the King Senator of the Kingdom of Italy. In 1903 he became chief of the Surgical Clinic of the University of Naples and occupied the office till death (Naples on December 21, 1913). His last years were saddened by a process because he left a gauze in the abdomen of a very sick cancer patient and for which he was completely acquitted by the tribunal of the parliament. His obituary was published in the year book of the University of Naples 1914-1915 where a total of 73 publications were listed. A monument has been erected by the municipality in Riesi, in front of his family house. For Spencer Watson he “was the greatest European Clinician” [13]. A street on the hill of city and a bust in the Department of Surgery honor him in Naples. On his death he was commemorated in the Senate. The President of the Italian Government, Giovanni Giolitti, presided the ceremony, the King sent a message.

Franz von Colmers
He was born in Berlin Charlottenburg in 1875. A child of Jewish parents, he studied medicine in Erlangen where he obtained his MD in 1899. He specialized in traumatology and war medicine and became assistant to Vincent Czerny in Heidelberg. He directed a Unit of the German Red Cross during the Russian-Japan War and in Sicily 1909 (although not in the forefront of the quake). Thereafter he became director of Surgery in Coburg Regional Hospital. In 1912 he was consultant to Queen Eleanor of Bulgaria for various hospitals in Sofia. With the advent of Nazism, being Jewish, he lost, in 1924, the position of surgeon in Coburg. From that year on he was in correspondence with Thomas Mann [17]. In 1935 he moved to Zurich and in 1936 he opened a surgical practice in New York. He died in 1960 in the Stanford Conn Hospital [18].

Rocco Caminiti
He was born in Villa San Giovanni in 1868. Medical studies were at the University of Messina. During the university studies he was attracted by comparative anatomy, histology, and zoology. He had as a tutor Professor Nikolaus Kleinenberg, a Baltic German zo-
ologist who collaborated with Dohrn in the venture of the Zoological Station in Messina and in Naples [19], MD, magna cum laude, on July 6, 1896. After the MD, he registered at the Faculty of Science and became a Ph.D.. He finally moved to the University of Rome where he worked under the direction of Marchiafava where he trained in bacteriology, morbid anatomy, and in the practice of autopsy in the years 1899-1902. In 1903 Antonio D’Antona offered him the position of assistant in surgery at the University of Naples where he obtained the venia legendi (reader in surgery) in surgery in 1905. In 1908 he was nominated director of surgery at the Loreto Hospital where he perfected his skill in laryngology and orthopedics. Later he was elected member of the National Senate national and mayor of Villa San Giovanni, where in the years 1920-1930 he started a private clinic bearing his name. It is still active and is managed by his grandchildren. The name and the fame of Rocco Caminiti are perpetuated in Villa San Giovanni by a Junior School and by a bust - gift of the Medical Society of Calabria - in Rosario Square.

Conclusion
The paper supports the notion that the crush syndrome was described years before Bywaters and Beall described it in 1941 and generated the wrong eponym Bywaters Syndrome. The syndrome of crush syndrome with acute renal failure was described by Antonino D’Antona in 1909 well before Bywaters [1] and of many other scientists [20] [23] [22] [23] [24] [25]. The crush syndrome without renal failure was described in 1909 by Colmers [7], D’Antona [10] [11] and by Rocco Caminiti. The data confirm and extend preliminary findings described elsewhere [26].

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