Editorial

Acute diseases, emergency admissions and mortality during weekends: should we be worried?

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A series of studies has reported a so called "weekend (WE) effect" for hospital admissions, referring to a higher risk for mortality for patients admitted on WE (Saturday to Sunday) than for those admitted on weekdays (WD). A lot of water has flowed under the bridge since, more than fifteen years ago, Bell & Redelmeier reported an association between WE admissions and significantly higher in-hospital mortality (IHM) rates for some acute diseases (1). Interestingly, a higher mortality risk has been reported either from the majority of studies dealing with severe life-threatening diseases, even top rank positioned among the established causes of sudden death (2), such as myocardial infarction and stroke (*Table 1*), and with many other kinds of admissions as well (*Table 2*). As for aortic disease, in particular, Bell & Redelmeier found that WE admissions were associated with significantly higher IHM rates than were WD admissions among patients with ruptured abdominal aortic aneurysms (42% *vs.* 36%, P<0.001), with an odds ratio (OR) of 1.28 (95% confidence interval, 1.13 to 1.46) (1). Two studies from our group, the former conducted on the population of the region Emilia Romagna of Italy (3), the latter on a comprehensive sample of cases of all the regions of Italy (4), confirmed that WE was an independent risk factor for IHM (OR 1.32, 95% confidence interval, 1.14 to 1.52, and OR 1.34, 95% confidence interval, 1.24 to 1.44, respectively). On the other hand, a series of negative findings also exist, and it has been argued that the so-called WE effect could not result in increased mortality but rather affect other quality of care parameters (5). The underlying causal mechanisms are uncertain, and possible concerns can be raised by the wide use of administrative archives as the main source of data, and by the preponderance of data collected in the United States, United Kingdom and Europe, and lack of data from other world regions (6). Among the factors called as a possible explanation for different findings regarding a WE effect (7), some plausible could be (I) suspected suboptimal standards of care and quality of care during WE; (II) differences in case-mix; and (III) disease-specific studies.

Suboptimal standard of care and quality of care

Several authors have called reduction in staffing and resources and presence of less experienced doctors as possible causes during WE, also due to the finding that hospitals with admitting consultant presence for a minimum of 4 h per day, had lower adjusted case fatality rates, including the ratio of WE/WD mortality (8). Understaffing is not to be intended as limited to doctors, but refers to nursing staff as well. It has been reported that the risk of death for stroke was higher in the case of a low nurse/bed ratio, and independent of rounds by specialist physicians (9). Studies on possible understaffing led the UK Government to be committed to working with the National Health Service to provide hospital care service with 7-day activity by 2020 (https://www.gov.uk/government/publications/7-day-nhs-services) (10).

Table 1 Weekend *vs.* weekday mortality risk in worldwide studies on myocardial infarction and stroke

Acute disease	Author, country, reference	Cases (n)	OR/HR
Myocardial infarction	Kostis *et al*., USA, N Engl J Med 2007	59,786	1.28
	Matsui *et al*., Japan, Circ J 2007	4,805	NS
	Hong *et al*., South Korea, Circ J 2010	97,466	1.21
	Hansen *et al*., Denmark, Int J Cardiol 2013	92,164	1.13
	Sneider *et al*., The Netherlands, Int J Cardiol 2013	6,820	NS
	O'Neill *et al*., Canada, Eur Heart J Acute Cardiovasc Care 2014	11,981	NS
	Isogai *et al*., Japan, Int J Cardiol 2015	111,200	1.22
	Agrawal *et al*., USA, Am J Cardiol 2016	3,625,271	1.02
Stroke	Saposnik *et al*., Canada, Stroke 2007	26,676	1.17
	Crowley *et al*., USA, Stroke 2009	13,821	1.14
	Fang *et al*., Canada, Neurology 2010	20,657	1.12
	Hoh *et al*., USA, Stroke 2010	599,087	NS
	McKinney *et al*., USA, Stroke 2011	134,441	1.05
	Palmer *et al*., USA, Arch Neurol 2012	93,621	1.18
	Niewada *et al*., Poland, Neurol Neurochir Pol 2012	19,667	1.13
	Albright *et al*., USA, Cerebrovasc Dis 2012	88,581	NS
	Inoue *et al*., Japan, J Stroke Carebrovasc Dis 2015	47,885	NS
	Cho *et al*., South Korea, J Stroke Cerebrovasc Dis 2016	8,957	1.22

OR, odds ratio; HR, hazard ratio; NS, not significant.

Differences in case-mix

More patients are admitted on WD than at WE, and a higher proportion of patients are admitted during WE through the emergency department, therefore patients admitted at WE could have increased illness severity and altered case mix (11). Nanchal *et al.* reported a 19% increased risk of death in patients admitted on WE for pulmonary embolism (12), and the hypothesis of a higher severity could be strengthened by the existence of several parameters of severity, such as need for mechanical ventilation, thrombolytic therapy use, and use of vasopressors (13).

Disease-specific studies

WE effect appears to be related to mortality especially in conditions at high risk of death immediately following the onset of acute disease, and timely interventions could impact survival. A large study analyzing the database of the US Nationwide Inpatient Sample, reported a reduction over time of the WE effect for myocardial infarction, with a progressive reduction over time from years 2000–2002 (OR 1.10) and 2003–2005 (OR 1.11), and a disappearance in 2006–2008 (OR 1.02, not significant) (14).

In a recent elegant article in *Lancet*, Walker and colleagues provided novel and interesting evidence with their study on 503,938 emergency admissions to four Oxford University National Health Service hospitals, UK 2006–2014, with a primary outcome of evaluating in- or out-of-hospital death within 30 days of admission (15). The authors designed several models, considering the effect of adjusting for 15 common haematology and biochemistry test results (haemoglobin, platelets, lymphocytes, neutrophils, eosinophils, monocytes, C-reactive protein, urea, bilirubin, creatinine, albumin, alanine aminotransferase, alkaline phosphatase, sodium, and potassium) using the closest result to admission time within 2 days before or after admission. The main results of this study were that 4.7% of WD and 5.1% of WE emergency admissions, respectively, died within 30 days

Table 2 Weekend *vs.* weekday mortality risk in worldwide studies on acute selected or unselected admissions (in alphabetical order)

Author, country, reference	Type of considered admission	Cases (n)	OR/HR
Selected			
Gallerani *et al*., Italy, Int J Cardiol 2011	Acute heart failure	9,657	1.33
James *et al*., Canada, J Am Soc Nephrol 2010	Acute kidney injury	214,962	1.07
Deshmukh *et al*., USA, Am J Cardiol 2012	Atrial fibrillation	86,497	1.23
Weeda *et al*., USA, Int J Cardiol 2016	Atrial fibrillation	78,847	1.02
Clarke *et al*., Australia, Inter Med J 2010	Chronic obstructive pulmonary disease	30,522	NS
	Acute myocardial infarction	17,910	1.15
	Hip fracture	4,183	NS
	Intracerebral haemorrhage	1,781	NS
Brims *et al*., United Kingdom, Clin Med (Lon) 2011	Chronic obstructive pulmonary disease	9,915	2.89
Goldstein *et al*., USA, J Pediatr Surg 2014	Pediatric surgery	439,457	1.63
Patel *et al*., United Kingdom, Br J Psychiatry 2016	Psychiatric admissions	45,264	NS
Powell *et al*., USA, J Emerg Med 2013	Sepsis	114,611	NS
Rumalla *et al*., USA, Clin Neurol Neurosurg 2017	Traumatic subdural hematoma	404,212	1.11
De Groot *et al*., The Netherlands, Aliment Pharmacol Ther 2012	Upper gastrointestinal bleeding	571	2.68
Unselected			
Marco *et al*., Spain, Am J Med Qual 2010	Admissions to internal medicine wards	429,880	1.10
Huang *et al*., Taiwan, Medicine (Baltimore) 2016	Admissions to internal medicine wards	82,340	1.19
Ozdemir *et al*., United Kingdom, Br J Anaesth 2016	General surgery admissions	294,602	1.11
Aylin *et al*., United Kingdom, Qual Saf Health Care 2010	All emergency admissions	4,317,866	1.10
Mikulich *et al*., Ireland, Acute Med 2011	All emergency admissions	49,337	1.11
Handel *et al*., United Kingdom, BMJ Open 2012	All emergency admissions	5,271,327	1.27
Sharp *et al*., USA, Am J Emerg Med 2013	All emergency admissions	4,225,973	1.07
Smith *et al*., United Kingdom, Emerg Med J 2014	All emergency admissions	20,072	1.07
Roberts *et al*., United Kingdom, Lancet 2015	All emergency admissions	30,668,050	1.096 England; 1,087 Wales
Barba *et al*., Spain, Eur J Intern Med 2016	All emergency admissions	35,993	1.40
Meacock *et al*., United Kingdom, J Health Serv Res Policy 2017	All emergency admissions	4,656,586	1.21
Conway *et al*., Ireland, QJM 2017	All emergency admissions	82,368	1.15

OR, odds ratio; HR, hazard ratio, NS, not significant.

(P<0.0001). Moreover, 9,347 patients underwent 9,707 emergency admissions on public holidays of whom 5.8% died within 30 days (P<0.0001 *vs.* weekday). The analyzed 15 routine haematology and biochemistry test results were highly prognostic for mortality, since adjustment for test results and standard patient features explained 33% of the excess mortality associated with emergency admission on Saturdays compared with Wednesdays, 52% on Sundays, and 87% on public holidays. Interestingly, despite previous suggestions of the responsibility role played by reduced staffing for excess mortality risk associated with WE admissions, this study did not find any association with mortality and staffing levels and service provision relative to each specific day of the week.

Moreover, Walker and colleagues found that mortality risk differed significantly by admission hour, being lowest at 8–11 AM. Authors reported that circadian variation in mortality risk was as great as (if not greater than) differences in risk between WE and WD. Adding admission hour significantly improve both the statistical models used, and excess mortality risk associated with WE admissions was somewhat greater between 8 AM and midnight, particularly between 11 AM and 3 PM, and somewhat less for admissions from midnight to 8 AM (15).

Such close relationship between time and onset and severity of certain acute diseases is extremely intriguing and fascinating. The cardiovascular system, and most cardiovascular functions, are organized according to a specific circadian order. Since circadian pattern is rhythmic, predictable-in-time differences in the physiological status of the cardiovascular system give rise to rhythmic variations in the susceptibility of human beings to morbid and mortal events (16). On the other hand, the pathological mechanisms of cardiovascular disease themselves exhibit temporal changes in both their manifestation and severity, leading to predictable-in-time differences in their ability to precipitate and graduate the overt expression of disease (16). It is already well known that the occurrence of cardiovascular events is not evenly distributed in time, but shows peculiar temporal patterns that vary with time of the day, the day of the week, and the month of the year. Due to temporal variation in the (I) pathophysiological mechanisms that trigger cardiovascular events and (II) physiological changes in the body rhythms, it is possible that several factors, not harmful if taken alone, may trigger unfavorable events when presenting all together at the same time (chronorisk) (16). Myocardial infarction, for example, exhibits highest frequency of onset during morning hours (6–12 AM). It has been estimated that the incidence rate of acute myocardial infarction (AMI) onset is 40% higher in the morning period than throughout the rest of the day, and nearly 28% of morning infarctions and 22% of sudden cardiac deaths (accounting for approximately 9% and 7% of all AMIs and sudden deaths, respectively), are attributable to the morning excess (17). Moreover, it is possible that time-dependent differences in clinical outcome may be present as well. During 6 AM–noon period, a trend toward a higher frequency of fatal cases was also shown (41.5% *vs.* 35.2%), independent of age, infarct site, and peak levels of MB creatine-kinase (18). Moreover, a retrospective cohort study conducted in 1,946 consecutive acute coronary syndrome (ACS) admissions to assess presenting clinical variables in patients admitted on days *vs.* nights and WD *vs.* WE found that there were fewer ACS admissions than expected on nights and WE (P<0.001), but the proportion of patients with ACS presenting with ST-elevation myocardial infarction (STEMI) was 64% higher on WE (P<0.001) and 31% higher on nights (19). This could explain higher mortality during morning hours and WE.

Walker and colleagues added an important piece to the discussed puzzle of emergency admissions and WE effect (15). They found that 33–52% of the residual excess mortality associated with WE admissions, and 87% of the excess mortality associated with emergency admissions during public holidays, could be explained by results of the selected 15 blood test results. Moreover, mortality was not associated with hospital workload or availability of levels of either staffing and services, and rather differences in clinical conditions of patients admitted during WE compared to WD could contribute to determine worst outcome (15).

Further researches are certainly needed to more-in-depth investigate the underlying factors of the so-called WE effect, and we maybe should keep in our mind that worst outcome could also depend of endogenous factors, including disruption of circadian rhythms (20).

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Footnote

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