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ORIGINAL RESEARCH ARTICLE

Prevalence and Risk Factors Associated with Use of QT-Prolonging Drugs in Hospitalized Older People

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Abstract

Aims The objective of this study was to evaluate the prevalence of the prescription of QT-prolonging drugs at hospital admission and discharge and the risk factors associated with their use in older people (aged 65 years and older).

Methods Data were obtained from the REPOSI (REgistro POliterapie SIMI [Società Italiana di Medicina Interna]) registry, which enrolled 4035 patients in 2008 ($n = 1332$), 2010 ($n = 1380$), and 2012 ($n = 1323$). Multivariable logistic regression was performed to determine the risk factors independently associated with QT-prolonging drug use. QT-prolonging drugs were classified by the risk of Torsades de Pointes (TdP) (definite, possible, or conditional) according to the Arizona Center for Education and Research on Therapeutics (AzCERT) classification. Specific drug combinations were also assessed.

Results Among 3906 patients prescribed at least one drug at admission, 2156 (55.2 %) were taking at least one QT-prolonging drug. Risk factors independently associated with the use of any QT-prolonging drugs were increasing age (odds ratio [OR] 1.02, 95 % CI 1.01–1.03), multimorbidity (OR 2.69, 95 % CI 2.33–3.10), hypokalemia (OR 2.79, 95 % CI 1.32–5.89), atrial fibrillation (OR 1.66, 95 % CI 1.40–1.98), and heart failure (OR 3.17, 95 % CI 2.49–4.05). Furosemide, alone or in combination, was the most prescribed drug. Amiodarone was the most prescribed drug with a definite risk of TdP. Both the absolute number of QT-prolonging drugs (2890 vs. 3549) and the number of patients treated with them (2456 vs. 2156) increased at discharge. Among 1808 patients not prescribed QT-prolonging drugs at admission, 35.8 % were prescribed them at discharge.

Conclusions Despite their risk, QT-prolonging drugs are widely prescribed to hospitalized older persons. The curriculum for both practicing physicians and medical students should be strengthened to provide more education on the appropriate use of drugs in order to improve the management of hospitalized older people.

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REPOSI denotes the REgistro POliterapie SIMI (Società Italiana di Medicina Interna); the full list of contributors is available online as Electronic Supplementary Material.

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Key Points

QT-prolonging drugs are largely prescribed in hospitalized elderly people.

Several risk factors were found to be independently associated with the use of QT-prolonging drugs in hospitalized elderly people.

The number of elderly patients treated with QT-prolonging drugs and the number of these medications prescribed dramatically increased at hospital discharge.

1 Introduction

Long QT syndrome is characterized by an abnormally long QT interval on the electrocardiogram (ECG). The QT-interval prolongation may induce a polymorphic ventricular tachycardia called Torsades de Pointes (TdP), a potentially life-threatening event that can lead to sudden cardiac death [1]. This condition can be inherited (so-called congenital long QT syndrome) or can be induced by drug use (so-called acquired long QT syndrome): in this context, several patient-specific factors have been recognized in the literature that may contribute to the risk of TdP, such as abnormal levels of calcium, potassium and magnesium, bradycardia, hypothyroidism, and a previous diagnosis of heart disease [1]. The actual incidence of TdP that is induced by QT-prolonging drugs use is unknown; it is believed to be underreported because it was only recently recognized as a health concern. Drugs that have the potential to cause TdP are numerous and in the last two decades the list has been frequently updated on the basis of new evidence. The drugs on this list are widely used for many cardiovascular and non-cardiovascular indications [2]. The association between TdP and cardiovascular morbidity and mortality is well-established [3, 4] and has led to the market withdrawal or restricted use of several medications over the years. For instance, the recommendations for domperidone-containing medicines have recently been revised due to concerns about their cardiac effects and their use to relieve symptoms of nausea and vomiting is only recommended for a limited period of time [5]. A number of studies report a direct link between the use of QT-prolonging drugs and an increased risk of sudden cardiac [6, 7] or cardiovascular death [8]. Moreover, there is evidence that the concomitant administration of more than one QT-prolonging drug may further increase the risk of developing a QT interval prolongation and TdP [9–18].

Elderly people, especially those aged 80 years or more, are the fastest growing segment of the population [19]. Aging is usually associated with multimorbidity [19], which is commonly accompanied by polypharmacy: for instance, in Italy 1.3 million elderly people take more than ten drugs daily, with the highest intake in the age group between 75 and 84 years [20]. Our previous studies showed that the polypharmacy rate at hospital discharge is dramatically increased in comparison with hospital admission [21], with a related increased risk of exposure to potential drug–drug interactions [22]. Moreover, advanced age is one of several recognized risk factors for the development of TdP that is associated with QT-prolonging drug use [23]. Since much effort is now addressed towards improving both the quality of life of older people and the optimal allocation of National Health Service (NHS) resources, improving appropriate drug prescription could be useful in reaching these endpoints.

With this background in mind, this study aimed to bring the high prescription prevalence of commonly prescribed drugs known to be possibly associated with cardiovascular risk to the attention of physicians. Specifically, the aims of this study were to evaluate (i) the prevalence of the use of QT-prolonging drugs at hospital admission and discharge; and (ii) the risk factors associated with QT-prolonging drug use in elderly people admitted to Italian internal medicine and geriatric wards participating in the prospective REPOSI (REgistro POliterapie SIMI [Società Italiana di Medicina Interna]) registry.

2 Methods

2.1 Setting and Data Collection

This study was conducted in 87 internal medicine and geriatric wards participating to REPOSI, a collaborative and independent prospective registry of the Italian Society of Internal Medicine (SIMI), IRCCS Fondazione Cà Granda Policlinico Hospital, and the IRCCS–Istituto di Ricerche Farmacologiche "Mario Negri". Briefly, consecutive patients aged 65 years or more admitted to hospital during four index periods lasting 1 week at the beginning of each season, and each separated from the next by 3 months (usually in January, April, July, and October), were enrolled in the study runs carried out once every 2 years (2008, 2010, and 2012). Participation was voluntary and all patients provided signed informed consent. The registry design and main results have been described in detail elsewhere [24]. The principal data collected included socio-demographic factors, clinical parameters,

performance of basic activities of daily living according to the Barthel Index scale [25], patterns of co-morbidities according to the Cumulative Illness Rating Scale (CIRS) [26], and medications prescribed. In particular, the registry collected data on drug prescriptions at hospital admission, during hospital stay, and at discharge. In this present study we analyze the number of active substances, regardless of the number of prescriptions.

2.2 Classification of QT-Prolonging Drugs

QT-prolonging drugs were defined according to the Arizona Center for Education and Research on Therapeutics (AzCERT) classifications [2]. AzCERT clinical scientists designed a risk-stratification process (Adverse Drug Event Causality Analysis [ADECA]) in order to assess whether or not drugs cause QT prolongation and/or TdP. The AzCERT team conducts a rigorous and continuously updated evaluation for every drug using the information available from basic science and clinical evidence as obtained from the medical literature, the US Food and Drug Administration (FDA) label, the FDA summary basis of approval, an analysis of the adverse events reported to the FDA Adverse Event Reporting System (AERS), and reports or inquiries to CredibleMeds® (crediblemeds.org) [2]. Drugs that prolong the QT interval are also defined by the risk of TdP occurrence, as follows:

1. *Definite risk of TdP*: Substantial evidence supports the conclusion that these drugs ($n = 49$) prolong the QT interval and carry a risk of TdP.
2. *Possible risk of TdP*: Substantial evidence supports the conclusion that these drugs ($n = 67$) prolong the QT interval but there is insufficient evidence that they carry a risk of TdP.
3. *Conditional risk of TdP*: Substantial evidence supports the conclusion that these drugs ($n = 47$) prolong the QT interval and carry a risk of developing TdP only under certain known conditions (e.g., excessive dose or overdose, or being the index or interacting agent in a drug–drug interaction). Our analysis was based on data from CredibleMeds® on 26 September 2014. Combinations of QT-prolonging drugs were assessed according to different categories of TdP risk.

2.3 Statistical Analysis

Data were summarized as frequencies (%), means, and standard deviations or medians and interquartile ranges, as appropriate. Chi-square or *t* tests were performed to assess differences between patients prescribed and those not prescribed QT-prolonging drugs. Multivariable logistic regression was performed to determine clinical and demographic factors independently associated with the use of QT-prolonging drugs at admission. The prevalence of prescriptions of QT-prolonging drugs at discharge was calculated for those patients known to be alive at that time and who had been discharged home or to a nursing home. The Chi-square test or Fisher's exact test was used for comparison between prevalence at admission and discharge.

The International Classification of Diseases, 9th edition (ICD-9) codes for atrial fibrillation (427.31/427.32), heart failure (428, 785.5), myocardial infarction (410), hypertension (401-405), diabetes (250), bradycardia (427.81), hypothyroidism (243-244), hypocalcemia (275.41), hypokalemia (276.8), and hypomagnesemia (275) were used.

The analysis was performed using the SAS/STAT® software version 9.1 (SAS Institute Inc., Cary, NC, USA).

3 Results

3.1 QT-Prolonging Drugs at Admission

The main characteristics of the patients at hospital admission are reported in Table 1. Among 4035 patients from the REPOSI registry, 3906 (96.8 %) were prescribed at least one medication at admission, and among them 2156 (55.2 %) were prescribed at least one QT-prolonging drug (up to a maximum of five); nearly 30 % ($n = 615$) were prescribed at least two QT-prolonging drugs. Overall, 2890 QT-prolonging drugs, alone or in combination, were prescribed. Prescription of the QT-prolonging drugs was equal between the sexes and the mean age of patients receiving them was 80 years. The clinical and demographic factors independently associated with the use of any QT-prolonging drugs we found included increasing age (odds ratio [OR] = 1.02, 95 % CI 1.01–1.03), multimorbidity (defined as ≥5 diagnoses) (OR = 2.69, 95 % CI 2.33–3.10), and hypokalemia (OR = 2.79, 95 % CI 1.32–5.89), and the main diagnoses at admission included atrial fibrillation (OR = 1.66, 95 % CI 1.40–1.98) and heart failure (OR = 3.17, 95 % CI 2.49–4.05).

The most prescribed QT-prolonging drug classes were diuretics (1391 patients), with furosemide being the most prescribed active substance (Table 2), followed by proton pump inhibitors, with pantoprazole the only active substance known to carry this risk, and antiarrhythmics (306 patients) with amiodarone, which was also the most prescribed drug carrying a definite risk of TdP. The next most prescribed were the selective serotonin reuptake inhibitors (286 patients), particularly sertraline, while other antidepressant drugs were less frequently prescribed.

Table 1 Main characteristics of patients enrolled in the REPOSI (REgistro POliterapie SIMI [Società Italiana di Medicina Interna]) study in relation to QT-prolonging drug use at admission

Variables	QT-prolonging drug [*n* (%)]	No QT-prolonging drug [*n* (%)]	*p* value
Total	2156 (53.4)	1879 (46.6)	
Sex (Female)	1098 (50.9)	993 (52.8)	0.22
Age[a]	79.95 (7.2)	78.35 (7.5)	<0.001
Year of REPOSI			
2008	664 (30.8)	668 (35.5)	0.001
2010	737 (34.1)	643 (34.2)	
2012	755 (35)	568 (30.2)	
Number of drugs[b]	6 (5–8)	4 (2–5)	<0.001
0		129 (6.9)	
1	22 (1.0)	234 (12.4)	
2–4	492 (22.8)	886 (47.2)	
5–9	1346 (62.5)	589 (31.3)	
≥10	296 (13.7)	41 (2.2)	
Number of diagnoses[b]	6 (4–8)	4 (3–6)	<0.001
Barthel Index[b,c]	84 (47–100)	95 (74–100)	<0.001
Total dependence (0–24)	267 (17.9)	103 (11)	
Severe dependence (25–49)	160 (10.7)	77 (6.3)	
Moderate dependence (50–74)	208 (13.9)	177 (9.7)	
Mild dependence (75–90)	269 (18)	194 (16)	
No or negligible dependence (91–100)	587 (39.4)	690 (57)	
Co-morbidities			
Atrial fibrillation	601 (27.9)	254 (13.5)	<0.001
Heart failure	430 (19.9)	93 (5.0)	<0.001
Hypertension	1584 (73.5)	1263 (67.2)	0.02
Myocardial infarction	26 (1.2)	10 (0.5)	<0.001
Diabetes	626 (29.0)	435 (23.2)	<0.001
Risk factors			
Bradycardia	11 (0.5)	2 (0.1)	0.02
Hypothyroidism	181 (8.4)	112 (6.0)	0.002
Hypocalcemia	7 (0.3)	2 (0.1)	0.16
Hypokalemia	46 (2.1)	9 (0.5)	<0.001
Hypomagnesemia	0	0	

[a] Mean (standard deviation)

[b] Median (interquartile range)

[c] Data collected in 2010 and 2012

Twenty-five percent of patients were prescribed at least one drug with a definite risk of TdP; 12.5 % of these drugs were not prescribed in combination (Table 3 and Electronic Supplementary Material Table S1). Almost 70 % of patients were prescribed at least one drug with a conditional risk of TdP, and 25 % of these patients took them in combination with other QT-prolonging drugs (Table 3 and Electronic Supplementary Material Table S1). Furosemide, a drug with a conditional risk of TdP, was the active substance most frequently associated with another QT-prolonging drug (Table 4).

3.2 QT-Prolonging Drugs at Discharge

There were 3549 QT-prolonging drugs prescribed at hospital discharge (659 more than at admission). Among the 3841 patients alive at discharge, 2465 (64.2 %) were prescribed QT-prolonging drugs, a proportion significantly higher than that observed at admission ($p < 0.001$); of these patients, 65.2 % were prescribed one QT-prolonging drug and 34.8 % at least two. Hence, the number of patients prescribed QT-prolonging drugs and the number of these drugs prescribed both increased at hospital discharge.

Table 2 Patients enrolled in REPOSI (REgistro POliterapie SIMI [Società Italiana di Medicina Interna]) according to the most frequently prescribed QT-prolonging drugs

Drug	Admission ($n = 2156$)		Drug	Discharge ($n = 2465$)	
	n	%		*n*	%
Furosemide[a]	1364	47.2	Furosemide[a]	1526	43.0
Pantoprazole[a]	340	11.8	Pantoprazole[a]	399	11.2
Amiodarone[b]	216	7.5	Amiodarone[b]	232	6.5
Sertraline[a]	91	3.1	Levofloxacin[b]	208	5.9
Alfuzosin[c]	90	3.1	Ciprofloxacin[a]	126	3.6
Citalopram[b]	82	2.8	Sertraline[a]	101	2.9
Trazodone[a]	71	2.5	Alfuzosin[c]	84	2.4
Paroxetine[a]	57	2.0	Citalopram[b]	82	2.3
Escitalopram[b]	55	1.9	Haloperidol[b]	69	1.9
Quetapine[c]	53	1.8	Domperidone[b]	67	1.9
			Trazodone[a]	65	1.8
			Paroxetine[a]	59	1.7
			Quetiapine[c]	56	1.6
			Escitalopram[b]	50	1.4

QT-prolonging drugs are listed by frequency of prescription, from top (most often prescribed) to bottom (least often prescribed)

[a] Conditional risk of Torsades de Pointes

[b] Definite risk of Torsades de Pointes

[c] Possible risk of Torsades de Pointes

Table 3 Patients enrolled in REPOSI (REgistro POliterapie SIMI [Società Italiana di Medicina Interna]) by category of risk of Torsades de Pointes and number of QT-prolonging drugs

Risk of TdP	Drug	Admission ($n = 2156$)		Discharge ($n = 2465$)	
		n	%	*n*	%
Definite	None	1589	73.7	1669	67.7
	1	542	25.1	728	29.5
	≥2	25	1.2	68	2.8
Possible	None	1912	88.7	2234	90.6
	1	234	10.8	224	9.1
	≥2	10	0.5	7	0.3
Conditional	None	401	18.6	437	17.7
	1	1484	68.8	1651	67.0
	≥2	271	12.6	377	15.3

TdP Torsades de Pointes

Specifically, of 1808 patients not prescribed QT-prolonging drugs at admission who were discharged alive, 648 (35.8 %) were prescribed these drugs at discharge (Electronic Supplementary Material Table S2). Among 1464 (1529 total minus 65 who died) patients discharged alive who were prescribed with only one QT-prolonging drug, this drug was stopped in 184 (12.5 %), while in 313 (21.4 %) it was subsequently prescribed in combination (Electronic Supplementary Material Table S2). The most prescribed QT-prolonging drugs were still diuretics (1550 patients), in particular furosemide, followed by antibacterials (454 patients), with levofloxacin and ciprofloxacin being the most prescribed (Table 2).

The percentage of patients prescribed drugs belonging to the class of definite TdP risk increased to 32.3 % (vs. 26.3 % at hospital admission; $p < 0.001$) (Table 3); this increase was also evident for drugs taken in combination with other QT-prolonging drugs (Electronic Supplementary Material Table S1). The percentage of patients prescribed drugs belonging to the class of possible TdP risk decreased to 9.4 % from 11.2 % at hospital admission ($p = 0.02$) (Table 3). The proportion of patients prescribed at least one drug belonging to the class of conditional risk of TdP remained similar to that observed at admission (82.3 vs. 81.4 %; $p = 0.4$) (Table 3). Furosemide remained the active substance most frequently taken in combination with

Table 4 Combinations of QT-prolonging drugs according to the active substances at admission and discharge

Drug combinations (active substances)	Admission (*n*)	Drug combinations	Discharge (*n*)
Pantoprazole[a]–furosemide[a]	151	Pantoprazole[a]–furosemide[a]	171
Amiodarone[b]–furosemide[a]	124	Amiodarone[b]–furosemide[a]	140
Furosemide[a]–sertraline[a]	33	Furosemide[a]–levofloxacin[b]	96
Furosemide[a]–alfuzosin[c]	30	Furosemide[a]–sertraline[a]	45
Furosemide[a]–trazodone[a]	25	Furosemide[a]–ciprofloxacin[a]	40
Furosemide[a]–citalopram[b]	23	Furosemide[a]–alfuzosin[c]	39
Pantoprazole[a]–amiodarone[b]	19	Furosemide[a]–haloperidol[b]	33
Furosemide[a]–levofloxacin[b]	19	Furosemide[a]–citalopram[b]	28
Furosemide[a]–paroxetine[a]	18	Pantoprazole[a]–amiodarone[b]	27
Furosemide[a]–sotalol[b]	17	Furosemide[a]–trazodone[a]	25
Furosemide[a]–haloperidol[b]	15	Domperidone[b]–furosemide[a]	22
Domperidone[b]–furosemide[a]	14	Furosemide[a]–fluconazole[b]	21
Furosemide[a]–quetiapine[c]	14	Furosemide[a]–paroxetine[a]	21
Pantoprazole[a]–sertraline[a]	10	Furosemide[a]–sotalol[b]	20
Furosemide[a]–escitalopram[b]	10	Furosemide[a]–quetiapine[c]	18
		Pantoprazole[a]–levofloxacin[b]	17
		Furosemide[a]–escitalopram[b]	17
		Furosemide[a]–metronidazole[a]	17
		Amiodarone[b]–levofloxacin[b]	15
		Pantoprazole[a]–sertraline[a]	13
		Amiodarone[b]–ciprofloxacin[a]	12
		Pantoprazole[a]–ciprofloxacin[a]	10

[a] Conditional risk of Torsades de Pointes

[b] Definite risk of Torsades de Pointes

[c] Possible risk of Torsades de Pointes

other QT-prolonging drugs (Table 4); the association of furosemide with antibacterials such as levofloxacin and ciprofloxacin increased substantially at discharge (Table 4).

4 Discussion

Since advanced age is one of the recognized risk factors for the development of TdP in users of QT-prolonging drugs, this study aimed to analyze the data from the prospective REPOSI registry in order to quantify and characterize the use of QT-prolonging drugs in elderly patients admitted to internal and geriatric wards.

Despite the occurrence of drug-induced QT prolongation being largely unpredictable, this remains an interesting issue for clinical practice due to the fact that many individual risk factors are known to play a role in facilitating drug-induced TdP [23]. Despite this, we found that prescription of QT-prolonging drugs is still often associated with such risk factors such as advanced age, electrolyte disturbance (hypokalemia), and underlying heart diseases (atrial fibrillation and heart failure).

The observed high prevalence of patients treated at hospital admission with at least one of these drugs (55 % alone and 30 % in combination) suggests that drug-induced QT prolongation and the associated risk of TdP are underestimated by general practitioners. However, drug prescription patterns at admission may also reflect the prescribing choices and decisions of specialists or previous hospitalizations. These findings are in line with the study of Curtis et al. [27], who conducted a retrospective cohort analysis on an outpatient prescription database including 4.8 million patients, in which 22.8 % were prescribed at least one QT-prolonging drug, 9.4 % in combination. On the other hand, a low prevalence of concomitant use of two or more QT-prolonging drugs was shown by a nationwide report of the Italian Medicines Agency (Agenzia Italiana del Farmaco [AIFA]) in 2011, but the survey considered only drugs with a definite risk of TdP [28].

At hospital admission, the most prescribed QT-prolonging drug classes were diuretics, particularly furosemide, alone or in combination, which is associated with QT-related arrhythmias via its capacity to cause hypokalemia, followed by proton pump inhibitors (pantoprazole, with its ability to trigger hypomagnesemia) and

antiarrhythmics such as amiodarone, which was the most prescribed drug with a definite risk of TdP. Overall, 25 % of patients taking at least one QT-prolonging drug were prescribed with a drug carrying a definite risk of TdP.

In contrast to other studies [29], we showed the frequent prescription of pantoprazole, the only proton pump inhibitor within the list [2]. This new finding should not be surprising as the AzCERT list is continuously updated [2]. The risk of QT prolongation associated with pantoprazole deserves particular attention given that proton pump inhibitors are often prescribed inappropriately [30]. Furthermore, our study shows that pantoprazole was most often prescribed in combination with other QT-prolonging drugs so that physicians could avoid the risk of TdP by substituting the drug with another of the same therapeutic class. Despite furosemide and pantoprazole having a conditional risk of TdP, they were most frequently prescribed in combination and/or in combination with another drug carrying a possible or definite risk of TdP. Because furosemide is usually administered to treat severe conditions such as heart failure and the benefit of this prescription largely exceeds its risk, greater attention should probably be placed on the potential QT-prolongation risk of the co-prescribed drugs. While the drugs being taken at hospital admission reflect the prescription of general practitioners as well as patient adherence, the pattern at hospital discharge generally reflects the prescription trend of hospital physicians. We found that the number of patients treated with QT-prolonging drugs and the absolute number of QT-prolonging drugs both increased dramatically at discharge. In particular, the number of patients prescribed at least one drug carrying a definite risk of TdP increased to 29.5 %. Among patients with no QT-prolonging drugs prescribed at admission, one-third were prescribed at discharge with at least one. These findings show that even in a hospital setting, physicians are not fully cognizant of a potentially life-threatening drug-induced adverse event such as TdP. This finding is consistent with that of another European study that showed that 33.5 % of patients admitted to a Swiss internal medicine ward were treated with at least one drug with the potential to prolong the QT interval, and half were discharged with at least one more prescription [31].

Among the 1464 (1529 total minus 65 dead) patients discharged alive who were taking a QT-prolonging drug alone, 313 (21.4 %) with other QT-prolonging drugs. At discharge, levofloxacin and ciprofloxacin were the antibacterials most prescribed, alone and in combination, although levofloxacin was recently recognized to carry a definite risk of TdP [2, 29]. Moreover, haloperidol and domperidone, which both have a definite risk of TdP, were among the most frequently prescribed drugs at discharge, alone and in combination. The co-prescription of an antipsychotic drug with another drug of the same class with a risk of QT prolongation is in line with the findings of Vandael et al. [32], in which a high association between antipsychotics and other antipsychotics or antidepressants was found, perhaps because they conducted the study in six psychiatric hospitals in Belgium. In their study, the most frequent combination was with furosemide.

5 Strengths and Limitations

The major strength of this study is the multicenter prospective design of the REPOSI registry and the inclusion of patients in four different year periods, which enabled us to balance any seasonal effect. Moreover, the large number of participating centers makes the study representative of the overall Italian setting of internal medicine and geriatric hospital wards. On the other hand, some limitations must be discussed. First, the REPOSI registry did not collect ECG data. Second, electrolyte values, which identify some of the common risk factors for TdP with QT-prolonging drugs, were not taken at admission or at discharge. Finally, a slight trend of risk of in-hospital overall mortality, after adjusting for sex, age and risk factors, was found among patients prescribed with a combination of either two or more than two QT-prolonging drugs (2 vs. 0: OR = 1.93, 95 % CI 1.40–3.51; >2 vs. 0: OR = 2.48, 95 % CI 1.15–5.34). Despite this, we could not assess any relationship between QT-prolonging drug use and cardiovascular mortality, which was less than 1 % in our study. Furthermore, with respect to critically ill hospitalized patients affected by acute and chronic conditions that could potentially lead to death (such as sepsis, cachexia, and pneumonia), sudden cardiac death (the specific endpoint associated with QT prolongation) is usually underreported as the primary cause.

6 Conclusions

Due to the high prevalence of prescription of QT-prolonging drugs, both at hospital admission and discharge, this study demonstrate that potential TdP induced by QT-prolonging drugs is still a neglected issue for many physicians, including general practitioners, specialists, and hospital physicians. The educational curriculum for both practicing physicians and medical students should be strengthened with regards to the appropriate use of drugs and drug–drug interactions in order to improve the management of hospitalized older people usually treated with multiple drugs. Given our results, the management of TdP risk associated with the use of these drugs and their surveillance in the community still remains an open question that deserves further investigation.

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Compliance with Ethical Standards

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