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Arrhythmia in tumor lysis syndrome and associated in-hospital mortality: A nationwide inpatient analysis

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Abstract

Background: Tumor lysis syndrome (TLS) is a life-threatening oncologic emergency associated with fatal complications including arrhythmia. The epidemiology and mortality outcomes of arrhythmia in TLS are scarcely studied in the literature.

Methods: We used the National Inpatient Sample (NIS) to study the prevalence and outcome of arrhythmia in patients hospitalized with TLS (ICD-9 code 277.88) from 2009 to 2014. Baseline characteristics, burden of arrhythmia, and pertinent outcomes were analyzed. Multivariable regression analysis was performed to identify the impact of underlying malignancy in predicting TLS-related mortality.

Results: A total of 9034 cases of arrhythmia among 37 861 TLS patients were identified. More than half of the arrhythmia cases (67%) were found among white old (>65) males admitted to large bed size and urban teaching hospitals. Arrhythmic cohort showed higher frequency of comorbidities such as fluid-electrolyte disturbances, hypertension, congestive heart failure, renal failure, dyslipidemia, diabetes, pulmonary circulatory disorders, chronic pulmonary disease, coagulopathy, and deficiency anemia. The most common malignancies were leukemia, lymphoma, metastatic tumor, and solid tumor without metastasis. We found significantly higher odds of in-hospital mortality among patients with TLS compared to general inpatient population on unadjusted (OR 9.69, 95% CI: 9.27-10.13, $P < .001$) and adjusted (OR 4.62, 95% CI: 4.39-4.85) multivariable analyses. Overall in-hospital mortality (32% vs 21.3%), median length of stay (11 days vs 9 days), and hospital charges were higher among arrhythmic than nonarrhythmic patients.

Conclusion: With the availability of more advanced cancer therapy in the US, nearly one in four inpatient encounters of TLS had arrhythmia. Arrhythmia in TLS patients was associated with higher odds of mortality and increased resource utilization. Therefore, strategies to improve the supportive care of TLS patients plus timely

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diagnosis and treatment of arrhythmia are of utmost importance in reducing mortality and health-care cost.

KEYWORDS
arrhythmia, atrial fibrillation, dysrhythmia, cardiotoxicity, cardio-oncology, tumor lysis syndrome

1 | INTRODUCTION

Tumor lysis syndrome (TLS) is a life-threatening oncologic emergency that may occur spontaneously or as a consequence of cancer treatment initiation.[1-3] TLS complications can range from mild electrolyte derangement to severe renal failure, seizure disorders, cardiac arrhythmias, and death.[4] Cardiac arrhythmia is one of the severe complications of TLS resulting from electrolyte derangement.[5] Many anticancer therapies are known to alter normal heart rhythm; however, there are very little data on the epidemiology and outcomes of arrhythmia during TLS on a large scale. The development of arrhythmia in cancer patients is a poor prognostic factor and has been shown to negatively impact therapeutic outcomes in cancer patients.[6] However, the burden and impact of underlying malignancy in predicting arrhythmia-related mortality remain unknown in TLS. We aimed to assess the prevalence and trends of arrhythmia, underlying malignant and nonmalignant comorbidities, along with associated in-hospital mortality during TLS-related hospitalizations using a national discharge database.

2 | METHODS

2.1 | Data source

Data from the National (Nationwide) Inpatient Sample (NIS), a nationally weighted sample of hospital discharges in the United States (US), were queried from 2009 to 2014, to describe the prevalence of arrhythmia in TLS patients and to determine the odds of in-hospital mortality in various malignancy groups with vs without arrhythmia. The NIS is an administrative dataset generated by the Agency for Healthcare Research and Quality (AHRQ) from the data backed by participating states.[7] The NIS incorporates a stratified sample of 20% nonfederal US community hospitals which represent nearly 95% of the US population. When weighted, the NIS dataset provides nationwide estimates of over 35 million hospitalizations annually and comprised of patient-level data points, up to 25 discharge diagnoses, and up to 15 procedural diagnoses.

2.2 | Study population

The NIS database has been used effectively recently to study arrhythmia risk in various conditions.[8-10] TLS is defined as a massive tumor cell lysis with the release of large amounts of potassium, phosphate, and nucleic acids into the systemic circulation. We used International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes (ICD-9-CM code 277.88) to identify TLS patients with various underlying malignancies. Admissions were stratified to arrhythmia or nonarrhythmia using ICD-9 CM codes described earlier.[8] Data on demographic details including age, sex, race, insurance status, malignant and nonmalignant comorbidities, and hospital characteristics including bed size, location/teaching status, and regions were studied.

2.3 | Study outcomes

The primary outcome of the study included the overall prevalence and trends in arrhythmia among TLS admissions with a subgroup analysis to determine the frequency of subtypes of arrhythmia. The secondary outcome was independent odds of in-hospital mortality in TLS with arrhythmia as compared to without arrhythmia in various underlying malignancies.

2.4 | Statistical analysis

Discharge weights were used to achieve national estimates. Categorical and continuous data were described in number or percentage and median [interquartile range] and analyzed by Pearson chi-square test and Mann-Whitney *U* test, respectively. A two-tailed $P < .05$ was considered as a threshold for statistical significance. SPSS v24 (IBM Corp) and complex sample modules were utilized to complete statistical analyses using defined strata/cluster design.

3 | RESULTS

The present study, which derived from 37 861 TLS patients admitted during 2009-2014, is by far the largest analysis on the impact of various arrhythmia during TLS hospitalization. A total of 23.9% of (n = 9034) encounters with arrhythmia were identified out of 37 861 TLS-related hospitalizations. The trends in the prevalence of arrhythmia were stable with rates ranging from 19.8% to 25.8%, with the highest frequency recorded in 2014 (25.8%) (Figure 1A). Atrial fibrillation (13.6%) was the most common arrhythmia followed by ventricular tachycardia in 2.6% of patients (Figure 1B).

The TLS cohort with arrhythmia often consisted of older [median (interquartile range, IQR); 68 (58-76) vs 63 (52-73) years], white

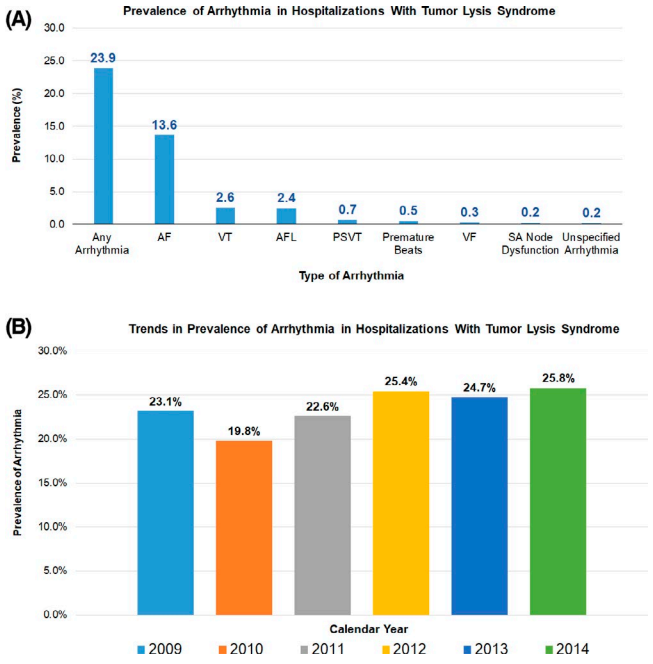

FIGURE 1 A, Prevalence of arrhythmia in hospitalizations with tumor lysis syndrome. B, Trends in prevalence of arrhythmia in hospitalizations with tumor lysis syndrome

(77.2% vs 69.7%), male (67.0% vs 62.6%) patients as compared to the cohort without arrhythmia (Table 1). Most of the arrhythmia cases occurred during nonelective admission (83.8%) in a large urban teaching hospital.

Comorbid conditions that are more likely to increase the risk of arrhythmia during TLS were studied. Fluid and electrolyte disorders were seen in two-third of the arrhythmic patients (72.8% vs 62.1%, $P < .001$). Of all 37 861 TLS-related admissions, 64.7% (n = 24 483) of patients had fluid-electrolyte disorders. Of these, 4.1% (n = 1007) of patients had conduction disorders. A total of 15 patients underwent pacing device placement or replacement among those having conduction disorders.

Other frequently observed comorbidities in the arrhythmic cohort include hypertension (50% vs 44.6%, $P < .001$), congestive heart failure (22.5% vs 9.9%, $P < .001$), dyslipidemia (24.5% vs 22.3%, $P < .001$), renal failure (22.8% vs 17.2%, $P < .001$), obesity (10.1% vs 8.5%, $P < .001$), diabetes mellitus (19.5% vs 16.8% $P < .001$), and previous MI PCI CABG (9.2% vs 6.1%) as compared to TLS cohort without arrhythmia. Pulmonary comorbidities associated with arrhythmia cases during TLS include pulmonary circulation disorders (7.8% vs 4.3%, $P < .001$) and chronic pulmonary disease (19% vs 13%, $P < .001$). Some of the hematological comorbidities associated with arrhythmic patients include coagulopathy (40.2% vs 36.1%, $P < .001$) and deficiency anemia (32.2% vs 32.1%, $P = .804$). Leukemia (46.3% vs 43.8%, $P < .001$), lymphoma (15.8% vs 12.8%, $P < .001$), metastatic cancer (10.3% vs 10.4%, $P < .001$), and solid tumors (4.4% vs 2.5%, $P < .001$) were the most common neoplasms associated with arrhythmia in TLS as compared to nonarrhythmics.

We found significantly higher odds of in-hospital mortality among patients with TLS compared to general inpatient population on unadjusted (OR 9.69, 95% CI: 9.27-10.13, $P < .001$) and adjusted (OR 4.62, 95% CI: 4.39-4.85) multivariable analyses.

In-hospital mortality rates were significantly higher among TLS patients with arrhythmia (32%) as compared to patients without arrhythmia (21.3%) (Table 2). Similarly, the median length of stay among TLS patients with arrhythmia was on average 2 days higher (11 days vs 9 days) than nonarrhythmic TLS patients. Arrhythmic patients were often stepped down from a hospital facility to SNF and ICF than nonarrhythmic TLS patients. Correspondingly, median hospitalization charges were significantly higher (USD 115 929 vs USD 89 704) among TLS patients with arrhythmia as compared to nonarrhythmic patients.

Multivariable analyses showed that TLS patients with solid tumor without metastasis (OR 5.12) followed by lymphoma (OR 2.23) had the highest risk of all-cause in-hospital mortality with arrhythmia as compared to without arrhythmia (Table 3).

4 | DISCUSSION

This is the first large-scale study demonstrating the prevalence, morbidity, and mortality of TLS patients developing arrhythmia. Nearly one in four TLS patients (23.9%) experienced arrhythmia during hospitalizations between 2009 and 2014, with the highest number of cases recorded in 2014 (25.8%). A higher prevalence of arrhythmia in TLS could be explained by the rapidly evolving and highly effective targeted cancer therapies, in which tumors that were once rarely associated with TLS are increasingly identified, which leads to increased risk of complications including arrhythmia owing to tumor shrinkage.[11,12] Atrial fibrillation (13.6%) is the most frequently reported arrhythmia in TLS patients. Other arrhythmias that were observed among TLS patients include ventricular tachycardia (2.6%) and atrial flutter (2.4%). Cancer patients are exposed to chemotherapy and radiation therapy, which has shown to induce structural changes in the heart, making the heart prone to the development of various arrhythmia.[13,14] Moreover, many anticancer therapies have been associated with cardiac rhythm changes which might increase the risk of arrhythmia during TLS.[15] Tamargo et al reported that the occurrence of arrhythmia was proven to be a poor prognostic factor and also was shown to impact the therapeutic outcomes of cancer patients.[6] The other known reason for the occurrence of arrhythmia during TLS is electrolyte disturbances.[5] In our study, we found that over two-third cases of arrhythmia (72%) to be associated with fluid and electrolyte disturbances. Cell death caused by actively proliferating cancer cells or treatment leads to cell lysis and release of various electrolytes leading to hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia, which may overwhelm the body's homeostatic mechanisms for excretion leading to electrocardiographic alterations and fatal arrhythmia.[4,5] Therefore, timely correction of electrolytes might prevent fatal arrhythmia in TLS.

TABLE 1 Baseline characteristics in hospitalizations with tumor lysis syndrome with vs without arrhythmia

Variables	No arrhythmia (N = 28 827)	Arrhythmia (N = 9034)	Overall tumor lysis syndrome (N = 37 861)	*P*
Age (years) at hospitalization				
Median [IQR]	63 [52-73]	68 [58-76]	65 [53-74]	**<.001**
18-44	15.1%	9.1%	13.7%	**<.001**
45-64	37.9%	29.0%	35.8%	
≥65	46.9%	61.9%	50.5%	
Sex				
Male	62.6%	67.0%	63.7%	**<.001**
Female	37.4%	33.0%	36.3%	
Race				
White	69.7%	77.2%	71.5%	**<.001**
African American	15.7%	12.1%	14.9%	
Hispanic	8.0%	5.9%	7.5%	
Asian or Pacific Islander	2.4%	1.6%	2.2%	
Native American	0.4%	0.2%	0.4%	
Others	3.7%	2.9%	3.5%	
Type of admission				
Nonelective	80.7%	83.8%	81.5%	**<.001**
Elective	19.3%	16.2%	18.5%	
Location/teaching status of hospital				
Rural	4.2%	4.0%	4.1%	.521
Urban non-teaching	17.6%	18.0%	17.7%	
Urban teaching	78.2%	78.1%	78.1%	
Comorbidities				
Alcohol abuse	1.9%	2.3%	2.0%	**.011**
Chronic blood loss anemia	0.9%	1.2%	0.9%	**.012**
Congestive heart failure	9.9%	22.5%	12.9%	**<.001**
Chronic pulmonary disease	13.0%	19.0%	14.4%	**<.001**
Coagulopathy	36.1%	40.2%	37.0%	**<.001**
Diabetes, uncomplicated	16.8%	19.5%	17.4%	**<.001**
Diabetes with chronic complications	3.6%	3.9%	3.7%	.172
Dyslipidemia	22.3%	24.5%	22.8%	**<.001**
Hypertension	44.6%	50.0%	45.8%	**<.001**
Valvular heart disease	2.7%	6.6%	3.7%	**<.001**
Previous MI/PCI/CABG	6.9%	9.2%	7.4%	**<.001**
Drug abuse	2.0%	1.4%	1.9%	**<.001**
Smoking	22.0%	21.3%	21.9%	.185
Hypothyroidism	9.1%	10.2%	9.4%	**.001**
Liver disease	5.6%	5.0%	5.5%	**.023**
Fluid and electrolyte disorders	62.1%	72.8%	64.7%	**<.001**
Other neurological disorders	4.9%	5.7%	5.1%	**.002**
Obesity	8.5%	10.1%	8.9%	**<.001**
Peripheral vascular disorders	3.3%	5.3%	3.8%	**<.001**
Pulmonary circulation disorders	4.3%	7.8%	5.1%	**<.001**
Renal failure	17.2%	22.8%	18.5%	**<.001**

(Continues)

TABLE 1 (Continued)

Variables	No arrhythmia (N = 28 827)	Arrhythmia (N = 9034)	Overall tumor lysis syndrome (N = 37 861)	*P*
Comorbid neoplasms				
Leukemia	43.8%	46.3%	44.4%	**<.001**
Lymphoma	12.8%	15.8%	13.5%	**<.001**
Multiple myeloma	5.2%	5.2%	5.2%	.961
Solid tumor without metastasis	2.5%	4.4%	3.0%	**<.001**
Metastatic cancer	10.4%	10.3%	10.4%	.716
Maintenance chemotherapy and radiotherapy	14.7%	9.6%	13.5%	**<.001**

Note: $P < .05$ (bold values) indicates statistical significance.

Abbreviations: CABG, coronary artery bypass grafting; HMO, health maintenance organization; IQR, interquartile range; MI, myocardial infarction; PCI, percutaneous coronary intervention.

TABLE 2 In-hospital outcomes in tumor lysis syndrome with vs without arrhythmia

Outcomes	No arrhythmia (N = 28 827)	Arrhythmia (N = 9034)	Overall tumor lysis syndrome (N = 37 861)	*P*
All-cause in-hospital mortality	21.3%	32.0%	23.9%	**<.001**
Disposition of patient				
Routine	44.0%	28.0%	40.1%	**<.001**
Transfer to short-term hospital	3.3%	3.4%	3.3%	
Other transfers (SNF, ICF, other)	12.4%	16.8%	13.5%	
Home health care	18.4%	19.1%	18.6%	
Length of stay (days), median [IQR]	9 [5-20]	11 [5-21]	10 [5-21]	**<.001**
Hospitalization charges (USD), median [IQR]	89 704 [43 159-196 596]	115 929 [53 549-224 444]	95 120 [45 244-203 778]	**<.001**

Note: $P < .05$ (bold values) indicates statistical significance.

Abbreviations: ICF, intermediate care facility; IQR, interquartile range; SNF, skilled nursing facility.

During 2009-2014, there were significantly two times higher rates of arrhythmia development in males than females. The higher rates of arrhythmia development in males have been reported in all age groups in many studies.[16-19] Our study reported two-third cases of arrhythmia during TLS among white people. Several studies have established a higher risk of arrhythmia occurrence in the white race.[20,21] Moreover, TLS patients aged > 65 were the most common age group prone to the development of arrhythmia during TLS in our study. Consistent with other studies, age and sex emerged as important and independent risk factors for rhythm changes during TLS.[22,23]

TABLE 3 Odds of in-hospital mortality in tumor lysis syndrome with vs without arrhythmia

Conditions	Adjusted odds ratio	95% confidence interval [lower-upper]	*P*
Overall tumor lysis syndrome	1.63	1.53-1.73	<.001
Leukemia	1.61	1.47-1.76	<.001
Lymphoma	2.23	1.89-2.64	<.001
Solid tumor without metastasis	5.12	3.42-7.66	<.001
Metastatic cancer	1.45	1.20-1.74	<.001
Multiple myeloma	1.53	1.09-2.14	.014

Note: $P < .05$ (bold values) indicates statistical significance.

Multivariable models were adjusted for age, sex, race, median household income, payer status, type of admission (elective-nonelective), hospital characteristics including bed size, location/teaching status and region, and baseline comorbidities mentioned in Table 1.

This study identified several important cardiac and extracardiac comorbidities that may contribute and increase the risk of arrhythmia development in TLS patients. The older age group has several cardiovascular comorbidities which might explain the higher risk of arrhythmia. This study revealed hypertension, dyslipidemia, smoking, diabetes, and heart failure to be significantly associated with TLS patients who developed arrhythmia. Heart failure has shown to confer the greatest magnitude of risk for arrhythmia, which might be explained by the changes in the heart structure and hence rhythm alterations in TLS and cancer-associated cardiomyopathy.[24] Similarly, hypertension and coronary artery disease, both known factors in the development of cardiac remodeling, were associated with rhythm abnormalities among TLS patients in our study.[25] Consistent with the

findings of this study, chronic pulmonary disease appeared to be associated with an increased risk of rhythm abnormalities in general.[26] Our findings highlight an association between higher frequency of smoking and arrhythmias in TLS patients. Some data suggest tobacco use to be associated with abnormal repolarization and arrhythmogenesis.[27]

Tumor lysis syndrome has been frequently observed in highly proliferative malignancies.[28] There are many subtypes of leukemia and lymphomas recorded in the literature associated commonly with TLS, including Burkitt's lymphoma, acute myeloid leukemia, chronic lymphocytic leukemia, low-grade lymphoma, and solid malignancies.[29-32] In our study, higher prevalence of arrhythmia was observed in leukemia patients. It is not uncommon to have leukemia associated with arrhythmia because of disturbances in heart rhythm caused by various electrolytes released secondary to cell death associated with highly proliferating cancer cells. Our study also found one-fourth of arrhythmia cases to be associated with lymphomas and metastatic cancer patients.

Moreover, a substantial increase in the hospitalization charges paid by Medicare (58.7%) was observed among arrhythmic patients compared to nonarrhythmic patients. Increased hospitalization charges among arrhythmic patients can be explained by another finding in our study that the duration of hospital stay among arrhythmics was longer than nonarrhythmic TLS patients. From 2009 to 2014, most of the arrhythmia cases (83.8%) were observed during nonelective admission in large bed-sized urban and teaching hospitals. One-fourth of arrhythmia cases in our study stepped down to a skilled nursing facility or intermediate care facility. The overall in-hospital mortality was higher among arrhythmia patients during TLS (32%) compared to nonarrhythmic TLS patients. The possible reason for these findings could be related to higher frequency of underlying cardiovascular comorbidities and in-hospital tumor-related complications, which might double the risk of mortality in TLS patients with arrhythmia. Another interesting finding in our study is that solid tumors without metastasis were associated with higher odds of in-hospital mortality. Increased odds of in-hospital mortality among these cancer patients is that a diagnosis of TLS in someone with a solid tumor would indicate a very high tumor burden, and thus an increase in the overall risk of mortality.[10] It is noteworthy to discuss here that acute kidney injury (AKI) in particular has been associated with high morbidity and mortality among TLS patients.[33] Therefore, its prevention requires early recognition, careful monitoring, and abrupt treatment of high-risk patients who developed signs of AKI.

As a result of recent advances in targeted therapy, prevalence and clinical significance of TLS and related complications are increasing. Our study has established a higher mortality bar among arrhythmia patients during TLS. Therefore, the most effective therapy in preventing arrhythmia during TLS remains the prevention. Recognition of high-risk patients, which our study has identified, is pivotal. Moreover, since various cancer therapies are associated with cardiotoxicity and arrhythmias, future clinical trials should monitor for possible EKG alterations and development of cardiac arrhythmia. Risk stratification of cancer patients is very important and there should be increased collaboration between oncologists and cardiologists under cardio-oncology specialty. Moreover, high-risk patients when identified must be monitored timely and treated before time to curb cardiac morbidity and mortality.

4.1 | Limitations

Our study should be viewed with few limitations. The NIS database increases the possibility of administrative coding errors and selection bias. The reason for arrhythmia development could not be identified based on the available ICD-9 codes. Furthermore, we could not differentiate admissions with new-onset vs preexisting arrhythmias using ICD-9 CM codes. The data on the duration of cancer and follow-up outcomes were not available. Furthermore, we cannot measure the severity of TLS and arrhythmia and therefore, the findings cannot be generalized to every TLS patient as the risk of arrhythmia and subsequent outcomes vary depending on the patient comorbidities, cancer type, and availability of healthcare resources. Though many studies have reported a higher risk of in-hospital mortality among TLS patients, we were not able to identify the specific cause of death. Because of the retrospective nature of the database, we could not study the period from the diagnosis of cancer to TLS development. The NIS database does not include information about anticancer medication, which could have increased the risk of arrhythmia development during TLS and related in-hospital mortality. Despite these limitations, the NIS is still the largest inpatient data source from the US providing national estimates.

5 | CONCLUSIONS

Our study has reported a nationwide prevalence, in-hospital complications, and mortality associated with arrhythmia in TLS patients. A timely recognition of high-risk cancer patients with TLS and prompt treatment will curtail fatal arrhythmia and associated in-hospital complications including the risk of mortality. Our findings in this critical but largely understudied subject warrant more attention by emerging cardio-oncologists and there is a dire need for planning of further prospective longitudinal investigations.

CONFLICT OF INTEREST

The authors declare no conflict of interests for this article.

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REFERENCES

1. Cortes J, Moore JO, Maziarz RT, Wetzler M, Craig M, Matous J, et al. Control of plasma uric acid in adults at risk for tumor lysis

syndrome: efficacy and safety of rasburicase alone and rasburicase followed by allopurinol compared with allopurinol alone–results of a multicenter phase III study. J Clin Oncol. 2010;28(27):4207–13.
2. Howard SC, Jones DP, Pui CH. The tumor lysis syndrome. N Engl J Med. 2011;364(19):1844–54.
3. McBride A, Westervelt P. Recognizing and managing the expanded risk of tumor lysis syndrome in hematologic and solid malignancies. J Hematol Oncol. 2012;5:75.
4. Howard SC, Pui CH. Pitfalls in predicting tumor lysis syndrome. Leuk Lymphoma. 2006;47(5):782–5.
5. Hochberg J, Cairo MS. Tumor lysis syndrome: current perspective. Haematologica. 2008;93(1):9–13.
6. Tamargo J, Caballero R, Delpon E. Cancer chemotherapy and cardiac arrhythmias: a review. Drug Saf. 2015;38(2):129–52.
7. HCUP Databases. Healthcare Cost and Utilization Project (HCUP). December 2019. Rockville, MD: Agency for Healthcare Research and Quality. [updated 2020 Mar 20]. Available from www.hcup-us.ahrq.gov/nisoverview.jsp
8. Desai R, Patel U, Deshmukh A, Sachdeva R, Kumar G. Burden of arrhythmia in recreational marijuana users. Int J Cardiol. 2018;264:91–2.
9. Desai R, Patel U, Sharma S, Amin P, Bhuva R, Patel MS, et al. Recreational marijuana use and acute myocardial infarction: insights from nationwide inpatient sample in the United States. Cureus. 2017;9(11):e1816.
10. Desai R, Rupareliya C, Patel U, Naqvi S, Patel S, Lunagariya A, et al. Burden of arrhythmias in epilepsy patients: a nationwide inpatient analysis of 1.4 million hospitalizations in the United States. Cureus. 2017;9(8):e1550.
11. Bose P, Qubaiah O. A review of tumour lysis syndrome with targeted therapies and the role of rasburicase. J Clin Pharm Ther. 2011;36(3):299–326.
12. Durani U, Shah ND, Go RS. In-hospital outcomes of tumor lysis syndrome: a population-based study using the national inpatient sample. Oncologist. 2017;22(12):1506–9.
13. Buza V, Rajagopalan B, Curtis AB. Cancer treatment-induced arrhythmias: focus on chemotherapy and targeted therapies. Circ Arrhythm Electrophysiol. 2017;10(8):e005443.
14. O'Neal WT, Lakoski SG, Qureshi W, Judd SE, Howard G, Howard VJ, et al. Relation between cancer and atrial fibrillation (from the REasons for Geographic And Racial Differences in Stroke Study). Am J Cardiol. 2015;115(8):1090–4.
15. Alexandre J, Moslehi JJ, Bersell KR, Funck-Brentano C, Roden DM, Salem JE. Anticancer drug-induced cardiac rhythm disorders: Current knowledge and basic underlying mechanisms. Pharmacol Ther. 2018;189:89–103.
16. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. JAMA. 1994;271(11):840–4.
17. Cameron A, Schwartz MJ, Kronmal RA, Kosinski AS. Prevalence and significance of atrial fibrillation in coronary artery disease (CASS Registry). Am J Cardiol. 1988;61(10):714–7.
18. Corrado D, Wichter T, Link MS, Hauer R, Marchlinski F, Anastasakis A, et al. Treatment of arrhythmogenic right ventricular cardiomyopathy/dysplasia: an international task force consensus statement. Eur Heart J. 2015;36(46):3227–37.
19. Linde C, Bongiorni MG, Birgersdotter-Green U, Curtis AB, Deisenhofer I, Furokawa T, et al. Sex differences in cardiac arrhythmia: a consensus document of the European Heart Rhythm Association, endorsed by the Heart Rhythm Society and Asia Pacific Heart Rhythm Society. Europace. 2018;20(10):1565–ao.
20. Khurshid S, Choi SH, Weng LC, Wang EY, Trinquart L, Benjamin EJ, et al. Frequency of cardiac rhythm abnormalities in a half million adults. Circ Arrhythm Electrophysiol. 2018;11(7):e006273.
21. Marcus GM, Olgin JE, Whooley M, Vittinghoff E, Stone KL, Mehra R, et al. Racial differences in atrial fibrillation prevalence and left atrial size. Am J Med. 2010;123(4):375.e1–7.
22. Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, Vasan RS, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. Circulation. 2004;110(9):1042–6.
23. Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. Circulation. 2006;114(2):119–25.
24. Roberts-Thomson KC, Lau DH, Sanders P. The diagnosis and management of ventricular arrhythmias. Nat Rev Cardiol. 2011;8(6):311–21.
25. McMurray JJ. Clinical practice. Systolic heart failure. N Engl J Med. 2010;362(3):228–38.
26. Oza N, Baveja S, Khayat R, Houmsse M. Obstructive sleep apnea and atrial fibrillation: understanding the connection. Expert Rev Cardiovasc Ther. 2014;12(5):613–21.
27. Ilgenli TF, Tokatli A, Akpinar O, Kilicaslan F. The effects of cigarette smoking on the Tp-e interval, Tp-e/QT ratio and Tp-e/QTc ratio. Adv Clin Exp Med. 2015;24(6):973–8.
28. Lotfi M, Brandwein JM. Spontaneous acute tumor lysis syndrome in acute myeloid leukemia? A single case report with discussion of the literature. Leuk Lymphoma. 1998;29(5–6):625–8.
29. Boccia RV, Longo DL, Lieber ML, Jaffe ES, Fisher RI. Multiple recurrences of acute tumor lysis syndrome in an indolent non-Hodgkin's lymphoma. Cancer. 1985;56(9):2295–7.
30. Cohen LF, Balow JE, Magrath IT, Poplack DG, Ziegler JL. Acute tumor lysis syndrome. A review of 37 patients with Burkitt's lymphoma. Am J Med. 1980;68(4):486–91.
31. Dizdar O, Yurekli BS, Purnak T, Aksu S, Haznedaroglu IC. Tumor lysis syndrome associated with fludarabine treatment in chronic lymphocytic leukemia. Ann Pharmacother. 2004;38(7–8):1319–20.
32. Zusman J, Brown DM, Nesbit ME. Hyperphosphatemia, hyperphosphaturia and hypocalcemia in acute lymphoblastic leukemia. N Engl J Med. 1973;289(25):1335–40.
33. Palevsky PM, Zhang JH, O'Connor TZ, Chertow GM, Crowley ST, Choudhury D, et al. Intensity of renal support in critically ill patients with acute kidney injury. N Engl J Med. 2008;359(1):7–20.

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