Retrospective Cohort Study of Association of NSAIDs Exposure and Outcome of Acute Decompensated Congestive Heart Failure

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Background and Objective: *Heart failure is a common medical disorder in elderly people. Previous studies have shown that non-steroidal anti-inflammatory drugs (NSAIDs) were considered to be associated with congestive heart failure (CHF) due to salt and water retention. However, there is limited data on NSAIDs-associated CHF in Thai population. The objective of the present study was to identify the significance of NSAIDs-related heart failure.*
Material and Method: *This is a retrospective cohort study. Patient's medical records with the diagnosis of CHF between January 2008 and December 2009 were reviewed. The authors divided patients with CHF into two groups according to history of NSAIDs-exposure within a one year prior to admission. Baseline characteristics were compared and Kaplan-Meier analysis was used to determine survival difference.*
Results: *One hundred ninety six CHF patients were included in the present study. NSAIDs-used within one year was confirmed in 47 patients (23.9%). Most of baseline characteristics were comparable for both groups. The major precipitating cause of CHF in NSAIDs-exposed group was statistically significant for acute coronary syndrome (40.4% vs. 14.8%, p-value <0.001), whereas anemia and renal failure failed to show statistical significance with p-value 0.859 and 0.370, respectively. Overall mortality showed no difference in both groups with p-value of 0.639.*
Conclusion: *Previous studies considered NSAIDs to be associated with CHF due to salt and water retention. However, in the Thai population, there was an increasing incidence of acute coronary syndrome in concomitant with decompensated CHF. Overall mortality in both groups was not significantly different.*

Keywords: *Congestive heart failure, Decompensated heart failure, Non-steroidal anti-inflammatory drugs, NSAIDs, NSAIDs-related heart failure, Acute coronary syndrome, Heart failure precipitating factors, Thai*

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Heart failure is a common medical disorder in elderly people. In Thailand, its mortality rate exceeded 18,399/100,000 population and was the third leading cause of death in 2010[1]. Congestive heart failure (CHF) is also on the top list of hospitalization causes. Previous study proved association between congestive heart failure and many precipitating factors including non-steroidal anti-inflammatory drugs[2,3]. This resulted in aggravating salt and fluid retention and was followed by congestive heart failure exacerbation[4,5].

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In 2010, one of the most imported medicines in Thailand was in the musculoskeletal group[6]. Among over-the-counter medicines, non-steroidal anti-inflammatory drugs (also known as NSAIDs) were the most popular drugs by far. The use of NSAIDs also increased every year due to rising incidence of osteoarthritis in the senior population.

However, the authors knew that NSAIDs would increase heart failure exacerbation but the authors could not identify patient's risk factors that might be associated with NSAIDs-induced heart failure yet. Previous studies have tried to find the association among these factors[7-9], such as, concurrent usage with high dose aspirin[10], impaired left ventricular systolic function (LVEF), dosage and duration of NSAIDs-used[11], history of upper gastrointestinal

hemorrhage[12], and history of chronic kidney disease, etc. Nevertheless, the authors still have very limited data of NSAIDs-related CHF, especially in the Thai population.

Material and Method

This is a retrospective cohort study. The primary objective of the present study was to identify mortality difference between CHF patients with and without NSAIDs-exposure. Secondary objectives were to find a difference in patients' characteristics between both groups and the significance of NSAIDs-related CHF.

Study population

The authors searched the database of Ramathibodi's Hospital (University-based hospital), matching ICD-10 that was associated with CHF (Table 1). One thousand three hundred two medical records with diagnosis relevant of congestive heart failure between January 1, 2008 and December 31, 2009 were found. Inclusion criteria for a non-exposed group (A) was patient age ≥15 with confirmed CHF. For exposed group (B), the patients have to be met above criteria plus evidence of NSAIDs exposure within one year.

At first, the authors reviewed the medical records that had the primary diagnosis of I50.0 (Congestive Heart Failure). However, after a hundred samples (n_1 = 206), there were only 7% of them that were exposed to NSAIDs within one year. Besides, we also identified many rejected medical records (mostly because there were no CHF events on admission or CHF events was a complication after admission). In addition, the difference in number of exposure would not have enough power to show the significance between exposed and non-exposed group.

Therefore, the authors decided to find more cases of NSAIDs associated CHF. This was based on Ramathibodi's medical records about ICD-10. Our medical residents assigned them online before the patients had been discharged. The assignment was based on individual basis. An example was that a patient with CHF, upper gastrointestinal hemorrhage (UGIB), and acute coronary syndrome (ACS) would have been assigned with UGIB as a primary diagnosis if the resident thought that was a major problem for the patient (even they might have concomitant CHF or ACS at the beginning).

As a result, even CHF was placed as a secondary diagnosis in the authors' ICD-10 database even if the patient might have been presented with CHF on admission. Therefore, the authors decided to match the data of NSAIDs prescription and ICD-10 diagnosis of CHF (regardless of primary or secondary diagnosis of ICD-10 in Table 2) to review them if they really have CHF event and/or were actually exposed to NSAIDs on admission.

After review (n_2 = 59), there were many crossovers to non-NSAIDs exposed group (if the authors found that NSAIDs prescription was not within one year prior to admission or was later to admission of CHF) and many rejected medical records.

Finally as disclosed in Fig. 1, one hundred forty nine records in the non-exposed group (A) were confirmed CHF with no known evidence of NSAIDs exposure. The second group was exposed group (B), which had 47 records of confirmed CHF and an evidence of NSAIDs used. List of NSAIDs available in the present study is shown in Table 2. Congestive heart failure was defined using "Framingham criteria for CHF" at the time of admission to the hospital.

Table 1. ICD-10 codes consistent with congestive heart failure

ICD-10	Description
I50	Heart failure
I50.0	- Congestive heart failure
I50.1	- Left ventricular failure
I50.9	- Heart failure, unspecified
I11.0	Hypertensive heart disease with heart failure
I13.0	Hypertensive heart disease with hypertensive kidney disease with heart failure
I13.2	Hypertensive heart disease with hypertensive kidney disease with heart failure and kidney failure

Table 2. List of NSAIDs available in our database

Type	Name
Conventional and partial selective COX-2 inhibitor	Diclofenac, DiclofenacInj, Ibuprofen, Indomethacin, Naproxen, Mefenamic acid, Piroxicam, Sulindac, Tenoxicam, Meloxicam
Selective COX-2 inhibitor	Etoricoxib, Celecoxib, ParecoxibInj

Individuals with age <15 years old, current pregnancy, diagnosis were not consistent with Framingham criteria for CHF. CHF that occurred after admission and patients whose medical records could not be retrieved for the first time were excluded from the present study.

If there were multiple admissions for those individuals, in non-exposure group, the authors would pick index admission date from the earliest admission in 2008 or 2009 (in order to show the longest course of disease and to increase sensitivity for detecting first episode of CHF). In exposure group the authors decided index admission date to be later admission to last dose of NSAIDs-prescribed (in order to document shortest duration of NSAIDs-used that might be associated with CHF).

Primary outcome

Primary outcome of the present study was all-causes mortality, which was calculated as the time from index CHF admission date to mortality date. Patients that did not show up on an appointment within six months were noted as loss to follow-up.

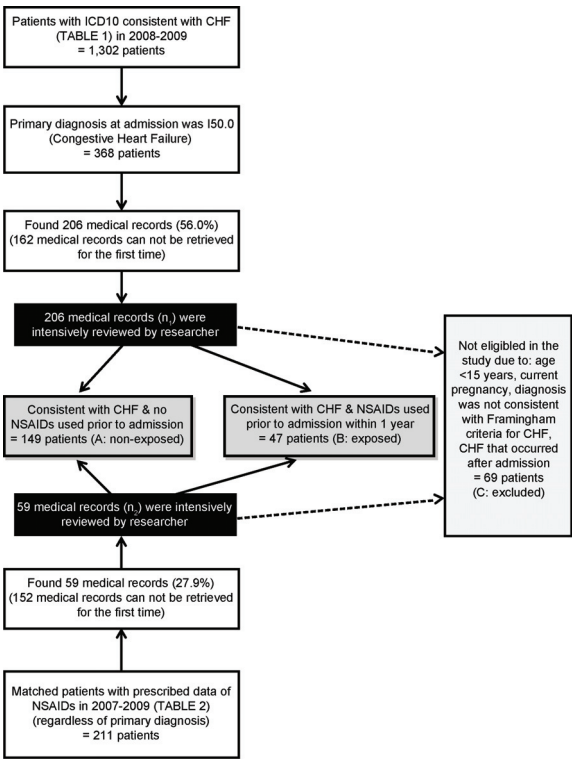

Fig. 1 Trial profile for patients enrolled in the study. CHF = congestive heart failure

Secondary outcome

Secondary outcomes were gathered as precipitating factors of CHF, including comorbidities on admission (such as acute coronary syndrome, acute kidney injury, and anemia), interventions given on admission (positive pressure ventilation or inotropic drug used), length of stays, and total hospital costs per day.

Identification of NSAIDs user

Evidence of NSAIDs used was defined as 1) Presence of Ramathibodi's prescription data of NSAIDs whose given date was prior to admission within 1 year. 2) Written NSAIDs usage within one year prior to admission in medical records (e.g., bought from local clinic). According to previous studies[7,8,11], the last dose of NSAIDs used for more than one year had not been shown to have a strong correlation with CHF.

Statistical analysis

Statistical analyses were performed using SPSS, version 11.5 (SPSS, Inc.; Chicago, Illinois). Parametric data were expressed as mean and standard deviation of the mean. Non-parametric data were expressed as median and interquartile range. The authors used Tests of independence (Pearson's Chi-square or Fisher's exact test) for categorical variables and Independent t-test (for mean) or Mann-Whitney method (for median) whenever appropriate to compare baseline characteristics/current drug-used/clinical presentations/precipitating factors on admission in both groups. Kaplan-Meier curves were used to determine survival difference. P-value less than 0.05 were taken as the threshold for statistical significance.

Ethical consideration

The researchers reviewed all medical records privately. The data remained unnamed and kept a secret. This study was approved by the ethics committee of Ramathibodi Hospital.

Results

Baseline characteristics of both group are shown in Table 3. One hundred ninety six patients were included in the present study. One hundred forty nine patients were in non-NSAIDs-exposed group and 47 patients were in NSAIDs-exposed group. Mean patient age was 68.5 years and most of them were male.

Table 3. Baseline characteristics of patients admitted with congestive heart failure

Variable	CHF without NSAIDs n = 149	CHF with NSAIDs n = 47	p-value	Overall n = 196
Age[a], years	68.64±15.61	68.23±13.59	0.872	68.55±15.11
Male	85 (57.0%)	26 (55.3%)	0.835	111 (56.6%)
1st admission of Heart failure	70 (47.6%)	26 (55.3%)	0.358	96 (49.5%)
Government insurance	88 (62.0%)	33 (71.7%)	0.229	121 (64.4%)
Universal coverage & others	54 (38.0%)	13 (28.3%)		67 (35.6%)
Functional status				
Class I	16 (12.0%)	11 (29.7%)	0.067	27 (15.9%)
Class II	66 (49.6%)	16 (43.2%)		82 (48.2%)
Class III	43 (32.3%)	9 (24.3%)		52 (30.6%)
Class IV	8 (6.0%)	1 (2.7%)		9 (5.3%)
History of coronary artery heart disease	59 (39.6%)	24 (51.1%)	0.165	83 (42.3%)
History of atrial fibrillation/flutter	39 (26.2%)	8 (17.0%)	0.200	47 (24.0%)
History of hypertension	114 (76.5%)	39 (83.0%)	0.350	153 (78.1%)
History of diabetes mellitus	71 (47.7%)	21 (44.7%)	0.722	92 (46.9%)
Average HbA1c[a], %	7.40±2.9	7.96±1.8	0.530	7.56±2.6
History of dyslipidemia	67 (45.0%)	28 (59.6%)	0.081	95 (48.5%)
History of gastrointestinal hemorrhage	17 (11.4%)	4 (8.5%)	0.575	21 (10.7%)
History of rheumatologic disease (e.g., osteoarthritis)	25 (16.8%)	17 (36.2%)	<0.005	42 (21.4%)
History of pulmonary disease	24 (16.1%)	11 (23.4%)	0.255	35 (17.9%)
History of vascular event (stroke/peripheral vascular disease)	26 (17.4%)	6 (12.8%)	0.449	32 (16.3%)
Average hematocrit[a], %	33.1±5.3	34.8±5.4	0.081	33.5±5.3
Average albumin[a], mg/dL	32.8±7.0	35.7±6.3	0.066	33.5±7.0
Average creatinine[b], mg/dL	1.40 (1.05-2.20)	1.20 (0.90-1.80)	0.089	1.4 (1.00-2.20)
Average LVEF[a], %	47.17±17.8	53.94±17.2	0.072	48.70±17.84
No aspirin used	84 (56.4%)	21 (45.7%)	0.140	105 (53.8%)
Low dose aspirin (≤100 mg/d)	36 (24.2%)	18 (39.1%)		54 (27.7%)
High dose aspirin (≥120 mg/d)	29 (19.5%)	7 (15.2%)		36 (18.5%)
Proton-pump inhibitor	43 (28.9%)	22 (47.8%)	0.017	65 (33.3%)

Data presented as quantitative and Chi-square, unless stated.
[a] Mean (SD of mean) and independent t-test
[b] Median (interquartile range) and Mann-Whitney
LVEF = left ventricular ejection fraction

From baseline characteristic above, it was found that both groups were comparable. However, NSAIDs-exposed group had a non-significant trend of better favorable characteristics than non-exposed group, including lower functional status (29.7% vs. 12.0%, p-value 0.067), higher LVEF (53.9% vs. 47.1%, p-value 0.072), higher hematocrit (34.8% vs. 33.1%, p-value 0.081), higher albumin (35.7 vs. 32.8 mg/dL, p-value 0.066), and lower creatinine (1.20 vs. 1.40 mg/dL, p-value 0.089). However, the patients in NSAIDs-exposed group also had a non-significant trend of higher dyslipidemia (59.6% vs. 45.0%, p-value 0.081).

Individuals with NSAIDs-exposed were found to have more musculoskeletal diseases (such as osteoarthritis and gout) and more proton-pump inhibitor usage (p-value <0.005 and 0.017, respectively).

Comorbidities and precipitating factors on admission are shown in Table 4. The major concomitant diseases with CHF are statistically significant for

Table 4. Comorbidities and precipitating causes of CHF on admission

Variable	CHF without NSAIDs n = 149	CHF with NSAIDs n = 47	p-value	Overall n = 196
Acute coronary syndrome[a]	22 (14.8%)	19 (40.4%)	<0.001	41 (20.9%)
Uncontrolled diet/fluid	39 (26.2%)	9 (19.1%)	0.329	48 (24.5%)
Non-compliant with medication/hemodialysis	11 (7.4%)	1 (2.1%)	0.415	12 (6.1%)
AKI/progressive CKD[b]	20 (13.4%)	4 (8.5%)	0.370	24 (12.2%)
Anemia any caused	35 (23.5%)	10 (21.3%)	0.859	52 (26.6%)
Anemia from UGIB[c]	5 (3.4%)	2 (4.3%)		
Asthma/COPD exacerbation	6 (4.0%)	5 (10.6%)	0.086	11 (5.6%)

[a] Defined as unstable angina, non-ST elevation myocardial infarction or ST elevation myocardial infarction.
[b] Defined as rising of serum creatinine >50%.
[c] Anemia defined as Hct ≤30%.
AKI = acute kidney injury; CKD = chronic kidney disease; UGIB = evidence of upper gastrointestinal hemorrhage; COPD = chronic obstructive pulmonary disease

acute coronary syndrome (ACS) in NSAIDs-exposed group (40.4% vs. 14.8%, p-value <0.001), whereas anemia and renal failure did not show any statistical significance with a p-value of 0.859 and 0.370, respectively. Asthma/chronic obstructive pulmonary disease exacerbation rate was also found to be higher in the NSAIDs-exposed group (10.6% vs. 4.0%, p-value 0.086).

NSAIDs use within one month prior to admission was identified in 15 CHF patients (7.65%). The most popular NSAIDs in the present study were celecoxib (21.2%) and diclofenac (19.1%) as shown in Table 5.

An inotrope/intraaortic balloon pump (IABP) usage and hospital costs per day had a non-significant tendency toward NSAIDs-exposed group with p-value of 0.082 and 0.099, respectively. Median hospital cost of patients' admitted with CHF was 5,114 baht per day. Overall mortality was not significantly higher in the NSAIDs group (14.9% vs. 12.1%, p-value 0.639). Ten patients were loss to follow-up in the present study. All of them were in non-exposed group as disclosed in Table 6. Kaplan-Meier curve for survival is shown in Fig. 2.

Table 5. NSAIDs data information in exposed group of CHF

Information	NSAIDs user, n = 47
Latest dose of NSAIDs used	
<7 days	9 (19.1%)
7 days-30 days	6 (12.7%)
>30 days-1 year	32 (68.0%)
Type of NSAIDs used	
Etoricoxib	6 (12.7%)
Celecoxib	10 (21.2%)
ParecoxibInj	2 (4.2%)
Diclofenac	9 (19.1%)
DiclofenacInj	2 (4.2%)
Ibuprofen	2 (4.2%)
Indomethacin	2 (4.2%)
Meloxicam	4 (8.5%)
Naproxen	7 (14.8%)
Mefenamic acid	1 (2.1%)
Piroxicam	2 (4.2%)
Sulindac	-
Tenoxicam	-

Discussion

Even with comparable baseline characteristics and significant rate of ACS event, the present study did not show a survival difference between the two groups. However, the survival curve shows an early separation. The authors thought that our population might be too little and follow-up time might be too short to identify a significant difference. A larger population and longer follow-up time is required for following trials.

Most of baseline characteristics were comparable. Some seemed to be non-significant better in NSAIDs-exposed group. The possible reason maybe because we would not prescribe NSAIDs to a patient with high-risk features in the first place (e.g., higher creatinine or previous UGIB). However, this should not misinterpret our baseline characteristics table. An example is that the authors could not conclude that PPI used simultaneously with NSAIDs increased rate of CHF because of p-value 0.017. It only confirms that there is a difference in PPI usage between these two groups, possibly due to ulcer prophylaxis.

NSAIDs-exposed group was found to have a significantly higher rate of acute coronary event

Table 6. Comparison of survivors and clinical severity between CHF patients with and without NSAIDs-exposed

Outcome	CHF without NSAIDs n = 149	CHF with NSAIDs n = 47	p-value	Overall n = 196
ETT or NIPPV used[a]	45 (30.4%)	17 (36.2%)	0.460	62 (31.8%)
Inotrope or IABP used[b]	10 (6.7%)	7 (14.9%)	0.082	17 (8.7%)
Length of stays[c], days	7 (4-11)	8 (5-13)	0.504	7 (4-12)
Costs per admission/day[c], baht	5,021 (3,273-8,556)	6,847 (3,269-7,745)	0.099	5,114 (3,722-16,955)
Survived	121 (81.2%)	40 (85.1%)	0.543	161 (82.1%)
Not survived	18 (12.1%)	7 (14.9%)	0.639	25 (12.8%)
Loss to follow-ups	10 (6.7%)	0 (0%)	0.068	10 (5.1%)
Follow-ups duration[c], weeks	63 (44-81)	65 (46-97)	0.426	63 (44-81)

[a] Endotracheal tube or non-invasive positive pressure ventilator used.
[b] Inotrope or intraaortic balloon pump used.
[c] Presented as median (interquartile range).

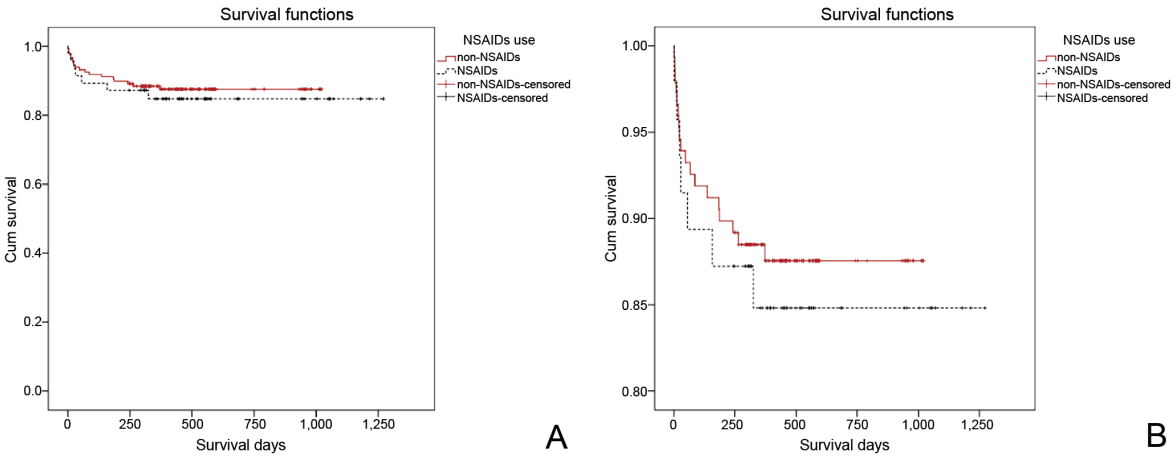

Fig. 2 Kaplan-Meier survival curve for distinguishing between CHF patients with and without NSAIDs-exposed (p-value 0.639).

that was concomitant with CHF. Even the baseline characteristic for history of coronary heart disease in both groups was not significant (p-value 0.165, Table 4). The result is consistent with previously known studies that NSAIDs-exposure would result in cardiovascular event. This is an interesting finding in a Thai population; because we made a hypothesis at first that NSAIDs would result in acute decompensate congestive heart failure (ADHF) via isolated mechanism of salt and water retention, which should be a short-term effect of NSAIDs. The authors expected this effect of NSAIDs to be within 30 days of exposure[13]. However, there were only 7.65% (15 patients) of short-term users identified in the present study population. This prevalence was in contrast with 22.1% in a previous case-control study[13]. Therefore, the majority of presented patients got CHF after being exposed to last doses of NSAIDs within one month to one year. Thus, this might represent a long-term effect of NSAIDs affecting Thai population apart from a short-term effect that has already been shown in Caucasian study. In addition, CHF exacerbation in this group was possibly precipitated by ACS event.

Nevertheless, the authors need more prospective trials regarding NSAIDs-effect on Thai people to determine if we are more susceptible to NSAIDs-induced ACS or are more tolerated to salt and water retention effects of NSAIDs. Besides, the authors made an assumption that trend of greater inotrope/IABP usage and hospital costs were due to higher ACS event in NSAIDs-exposed group. However, anemia and renal failure, which were important short-term side effects of NSAIDs, did not show any trend of significance.

Unexpectedly, concomitant asthma/COPD exacerbation had a trend to be higher in NSAIDs-

exposed group (p-value 0.086), even with no difference in underlying Asthma/COPD (p-value 0.255). The authors made a hypothesis that it could be due to cyclooxygenase pathway inhibition and increased leukotriene pathways synthesis. However, the authors need more evidence regarding this issue.

The major limitations of the present study are that the patients were not randomized and that we excluded patients whose medical records could not be retrieved for the first time (314 in 579 patients, 54.2%). Then there was a large number of patients who had not been included in the present study. The reason for not requesting medical records for the second time was that the authors were short of time. The authors could not use the online data of medical records in Ramathibodi's system to review as it may have an incomplete data and the authors do not have separate medical records for inpatient chart and outpatient chart. The authors have to do an intensive review traditionally, which took about two to three days for requesting their charts from medical record department and it took about 30 minutes for one medical record to be completely reviewed. Therefore, if we made multiple requests for unfound charts, it would have been time-consuming and would result in a longer study period.

The major reason for unfound medical records was because patient had an appointment around the time requested. Therefore, medical charts could not be retrieved for a few days before and after an appointment.

Furthermore, there was an inconclusive data of onset, type, and duration of NSAIDs use that was associated with CHF. Even previous studies showed no CHF effect when NSAIDs were used more than one year[7,8,11]. The latest dose of NSAIDs-exposed within one year in the present study may be too long to express the effect of salt and water retention. However, this may be an advantage in showing a long-term effect of NSAIDs as found in upcoming acute coronary event.

Another concern regarding this issue was the authors' protocol. Since we chose CHF patients that were admitted to the hospital but did not include mild CHF patients that were easily treated at OPD or ER, we might miss many CHF patients. Moreover, there is a limitation in documenting NSAIDs-usage from medical records retrospectively. Thus, there could possibly be some contaminations between the present study groups.

About multiple admission selection protocol, as the authors mentioned earlier that a number of NSAIDs users were too few in the authors population. Our primary outcome was to compare mortality between groups of NSAIDs user and non-user. Therefore, the authors had to identify more cases by selecting the admission that was related to NSAIDs.

Even if the patients were not randomized and had been selected from an unequal method, the authors did review their baseline characteristics, which shown no difference for most of parameters (p-value >0.05). Therefore, the authors suggested that our population was quite comparable between both groups and should be an acceptable pilot sample for a Thai population. However, in order to show mortality significance, further prospective trial with a larger population for this issue is mandatory.

Conclusion

From the previous studies, NSAIDs were considered to be associated with congestive heart failure due to salt and water retention. However, in a Thai population, there was an increasing incidence of acute coronary syndrome in concomitant with decompensated CHF when NSAIDs were used within one year. Overall mortality for both groups was not significantly different, but survival curve displaying early separation was observed. The authors need a larger population and a longer follow-up time for the next trials.

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Potential conflicts of interest

None.

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การศึกษาย้อนหลังเพื่อหาความสัมพันธ์ระหว่างการได้รับยาต้านการอักเสบที่ไม่ใช่สเตียรอยด์และการเกิดภาวะหัวใจล้มเหลวเฉียบพลัน

วิสุทธิ์ เกตุแก้ว, สุกิจ แย้มวงษ์, สุรกิจ นาทีสุวรรณ, ครรชิต ลิขิตธนสมบัติ

ภูมิหลัง: *ภาวะหัวใจล้มเหลวเป็นภาวะที่พบได้บ่อยในผู้สูงอายุ ซึ่งพบว่ามีปัจจัยภายนอกหลายอย่างที่สามารถกระตุ้นให้เกิดภาวะนี้ ได้จากการศึกษาที่ผ่านมาพบว่าการใช้ยาต้านการอักเสบที่ไม่ใช่สเตียรอยด์ สามารถกระตุ้นให้เกิดภาวะหัวใจล้มเหลวผ่านทางกลไกการคั่งของน้ำและเกลือแร่ อย่างไรก็ตามรายงานการศึกษาเกี่ยวกับระบาดวิทยาของภาวะหัวใจล้มเหลวที่เกิดจากยาต้านการอักเสบในประเทศไทยยังมีค่อนข้างจำกัด*

วัตถุประสงค์: *เพื่อศึกษาหาความเกี่ยวข้อง ระหว่างการใช้ยาต้านการอักเสบที่ไม่ใช่สเตียรอยด์และการเกิดภาวะหัวใจล้มเหลวโดยมีเป้าหมายหลักในการหาอัตราการเสียชีวิตในผู้ป่วยกลุ่มนี้เทียบกับกลุ่มที่ไม่ได้รับยามาก่อน*

วัสดุและวิธีการ: *การศึกษานี้เป็นการศึกษาแบบติดตามย้อนหลังในผู้ป่วยที่เข้ารับการรักษาตัวในโรงพยาบาลรามาธิบดี ระหว่างปี พ.ศ. 2551-2552 โดยศึกษาทบทวนจากเวชระเบียนผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นโรคหัวใจล้มเหลว โดยแบ่งผู้ป่วยหัวใจล้มเหลวออกเป็น 2 กลุ่ม คือกลุ่มที่ได้รับยาต้านการอักเสบที่ไม่ใช่สเตียรอยด์ภายในระยะเวลา 1 ปีก่อนที่จะมานอนโรงพยาบาล และกลุ่มที่ไม่เคยได้รับยาดังกล่าวมาก่อนเพื่อเปรียบเทียบอัตราการเสียชีวิตระหว่างผู้ป่วยทั้งสองกลุ่ม*

ผลการศึกษา: *จากการรวบรวมและวิเคราะห์ข้อมูลในผู้ป่วยทั้งหมดจำนวน 196 ราย พบว่าการแบ่งกลุ่มผู้ป่วยด้วยประวัติการใช้ยาต้านการอักเสบที่ไม่ใช่สเตียรอยด์ภายในระยะเวลา 1 ปีก่อนที่จะนอนโรงพยาบาล มีผู้ป่วยที่ใช้ยากลุ่มดังกล่าวจำนวนทั้งหมด 47 ราย (คิดเป็นร้อยละ 23.9) ซึ่งในผู้ป่วยทั้งสองกลุ่มนี้มีลักษณะพื้นฐานที่ไม่แตกต่างกัน*

สำหรับปัจจัยกระตุ้นที่พบบ่อยที่สุดในกลุ่มที่ใช้ยาต้านการอักเสบที่ไม่ใช่สเตียรอยด์ คือภาวะหัวใจขาดเลือดเฉียบพลัน โดยมีนัยสำคัญทางสถิติเมื่อเทียบกับอีกกลุ่มหนึ่ง คือพบได้ถึงร้อยละ 40.4 เทียบกับร้อยละ 14.8 ($p<0.001$) ส่วนผลข้างเคียงอื่น ๆ ของยาต้านการอักเสบที่ไม่ใช่สเตียรอยด์นั้นกลับพบว่าไม่ได้มีนัยสำคัญทางสถิติที่เพิ่มขึ้นอย่างชัดเจน เช่น ภาวะซีด ($p = 0.859$) หรือ ไตวายเฉียบพลัน ($p = 0.370$) ส่วนอัตราการเสียชีวิตนั้นพบว่าทั้งสองกลุ่มไม่มีความแตกต่างกัน ($p = 0.639$)

สรุป: *จากการศึกษาที่ผ่านมาพบว่าการใช้ยาต้านการอักเสบที่ไม่ใช่สเตียรอยด์มีผลกระตุ้นให้เกิดภาวะหัวใจล้มเหลวเฉียบพลันโดยผ่านกลไลการคั่งของน้ำและเกลือแร่ อย่างไรก็ตามจากการศึกษานี้ยังพบอัตราการเกิดร่วมของภาวะกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันเพิ่มขึ้นอย่างมีนัยสำคัญในผู้ป่วยไทยที่ได้รับยากลุ่มดังกล่าวในระยะเวลา 1 ปี และพบว่าอัตราการเสียชีวิตของผู้ป่วยทั้งสองกลุ่มไม่มีความแตกต่างกัน*