

The impact of pre-existing shoulder diseases and traumatic injuries of the shoulder on adhesive capsulitis in adult population

A population-based nested case-control study

Chung-Yuh Tzeng, MD, PhD^{a,b}, Hsiu-Yin Chiang, PhD^c, Chun-Che Huang, PhD^{d,e}, Wei-Szu Lin, MSc^e, Tzu-Hung Hsiao, PhD^{e,f}, Ching-Heng Lin, PhD^{e,f,g,h,*}

Abstract

Adhesive capsulitis (AC) is a common chronic disorder for adult patients; however, whether a history of pre-existing shoulder diseases may affect the development of AC is still not fully understood. We aimed to investigate the incidence and prevalence of AC and to assess the association of pre-existing shoulder diseases and traumatic injuries of the shoulder with the development of AC in adults.

This retrospective population-based cohort and nested case-control study used data from the National Health Institute Research Database of Taiwan. A total of 24,414 patients aged 20 years or older and with a diagnosis of AC were identified between 2000 and 2013. We calculated the incidence of AC for each year during the study period. In addition, these AC patients were matched with controls (n=97,656) in a ratio of 1:4 based on age, gender, and index date. Univariate and multivariate logistic regression models were performed to identify variables associated with AC.

Females and patients aged 50 to 69 years had higher age-gender standardized incidence and prevalence of AC than their counterparts. Multivariate analyses showed that after adjusting for relevant covariates, pre-existing shoulder diseases of calcific tendinitis (odds ratio [OR]=8.74, 95% confidence interval [CI]=5.66-13.5), biceps tendinitis (OR=7.93, 95% CI=5.33-11.79), rotator cuff syndrome (OR=6, 95% CI=5.26-6.85), osteoarthritis (OR=4.27, 95% CI=3.44-5.3), and impingement syndrome (OR=3.13, 95% CI=2.64-3.71), as well as fracture (OR=4.51, 95% CI=3.82-5.34) and dislocation (OR=3.57, 95% CI=2.35-5.45) of the shoulder were significantly associated with AC risk.

Higher odds of AC were observed among patients with pre-existing shoulder conditions. This study highlights the need to consider differences in AC risk among patients with various types of shoulder diseases and traumatic injuries of the shoulder.

Abbreviations: AC = adhesive capsulitis, AOR = adjusted odds ratio, CI = confidence interval, COR = crude odds ratio, ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification, IRR = incidence rate ratio, LHID = Longitudinal Health Insurance Database, NHI = National Health Insurance, NHIRD = National Health Insurance Research Database, NTD = new Taiwan dollars, OR = odds ratio, SD = standard deviation.

Keywords: adhesive capsulitis, case-control, comorbidities, incidence, prevalence, shoulder diseases

Editor: Phil Phan.

C-YT and H-YC contributed equally to this study.

This work was supported by the Taichung Veterans General Hospital in Taiwan (TCVGH-1057329D, TCVGH-105G213, and TCVGH-NHRI10505).

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

^a Department of Orthopedics, Taichung Veterans General Hospital, Taichung, ^b Department of Medicinal Botanicals and Health Applications, Da-Yeh University, Changhua, ^c Big Data Center, China Medical University Hospital, Taichung, ^d Department of Healthcare Administration, I-Shou University, Kaohsiung, ^e Department of Medical Research, Taichung Veterans General Hospital, Taichung, [†] Department of Public Health, Fu-Jen Catholic University, New Taipei, ^g Department of Health Care Management, National Taipei University of Nursing and Health Sciences, Taipei, ^h Department of Industrial Engineering and Enterprise Information, Tunghai University, Taichung, Taiwan.

* Correspondence: Ching-Heng Lin, Department of Medical Research, Taichung Veterans General Hospital, 1650 Taiwan Boulevard, Sector 4, Taichung City 40705, Taiwan (e-mail: epid@vghtc.gov.tw).

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How to cite this article: Tzeng CY, Chiang HY, Huang CC, Lin WS, Hsiao TH, Lin CH. The impact of pre-existing shoulder diseases and traumatic injuries of the shoulder on adhesive capsulitis in adult population. Medicine 2019;98:39(e17204).

Received: 3 April 2019 / Received in final form: 29 July 2019 / Accepted: 23 August 2019

http://dx.doi.org/10.1097/MD.000000000017204

1. Introduction

Adhesive capsulitis (AC) is a common shoulder disease that is also known as frozen shoulder. Approximately 2% to 5% of the general population suffer from AC.^[1,2] Patients with AC often experience mild to severe shoulder pain and have limited range of motion, which can cause substantial discomfort in patients and affect their quality of life.

AC can be subdivided into primary and secondary AC. Primary AC, also called idiopathic AC, can occur without any specific trauma or inciting event. Secondary AC usually happens after periarticular fracture dislocation of the glenohumeral joint, or other severe trauma (e.g., fracture over the shoulder joint, rotator cuff tear, or impingement syndrome).^[3] The secondary AC is categorized into systemic (diabetes mellitus and other metabolic disorders), extrinsic (cardiopulmonary disease, cervical disc disorders, and humerus fractures), and intrinsic factors (rotator cuff pathologies, biceps tendinopathy, calcific tendinopathy, and AC joint arthritis).^[4] However, the exact pathogenesis of AC remains uncertain.

The treatment of AC includes medications and physical therapy.^[5–7] Previous studies have shown the treatment effect of rehabilitation, acupuncture, intra-articular steroid injection,^[8] manipulation under anesthesia, and arthroscopic intracapsular release on improving AC.^[9] However, most treatments are of limited effectiveness in changing the natural course of the condition. Most patients can recover within 2 years, but some patients cannot tolerate the disability of shoulder joint due to pain and limited range of motion and seek for surgical treatment.^[10]

Comorbidities such as diabetes mellitus or thyroid disorders are known to be associated with AC.^[11–14] A cohort study from Taiwan reported that diabetic patients had a 32.1% higher risk of acquiring AC within 3-year follow-up, compared with nondiabetic patients.^[11] Austin et al investigated the association between metabolism syndrome markers and AC and they confirmed that hyperglycemia was associated with AC. They also found possible associations between hypertension, proinflammatory condition, certain metabolic syndrome, and AC.^[14]

To date, only a few studies have investigated the demographic and clinical characteristics of AC in Asian populations meaning that the data may not be applicable to western subjects due to influence from changing environmental and social factors.^[15] However, the evidence of difference in AC between Asian and non-Asian countries is inconclusive.^[15,16] In addition, medical comorbidities (e.g., diabetic mellitus, hypertension, or thyroid disease)^[11–14] or shoulder diseases (e.g., calcified tendinitis or rotator cuff diseases^[10]) have been noted in patients with AC. However, the magnitude of these factors was not well evaluated using robust methods for observational data. Therefore, this study aimed to investigate the incidence and prevalence of AC in a Taiwanese population-based cohort study; to assess the association of pre-existing shoulder diseases and traumatic injuries of the shoulder with the development of AC in a nested case-control study.

2. Materials and methods

2.1. Data source

The National Health Insurance (NHI) program is a mandatory universal health insurance that covers over 99% of the

population (23 million people) in Taiwan. The National Health Insurance Research Database (NHIRD) comprises comprehensive administrative and claims data of all NHI beneficiaries. We used a representative subset of the NHIRD known as the Longitudinal Health Insurance Database (LHID), which consisted of 1,000,000 randomly selected subjects from the 23 million beneficiaries who were covered by NHI. There were no significant differences in distribution of age, gender, and average insured payroll-related premiums between LHID and NHIRD samples. To protect data privacy and security, the National Health Research Institute has encrypted all personal identification numbers before releasing the data. All diagnoses were identified using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. In addition, this study was approved by the Institutional Review Board of the Taichung Veterans General Hospital (approval no. CE13152B-5). Written informed consent was waived because of the retrospective use of patient data.

2.2. Study population

This study used a retrospective cohort design to estimate the annual incidence and prevalence of AC between 2000 and 2013. To increase diagnostic accuracy, we identified patients who had a diagnosis of AC of shoulder (ICD-9-CM 726.0) for at least 3 outpatient visits or at least 1 inpatient admission during the study period. The index year was the year of the first AC diagnosis.

In addition, this study also used a nested case-control design to identify the factors associated with AC. First, we divided the cohort into 2 groups: patients with AC diagnosis during any visit or admission and patients without any AC diagnosis. Second, from the AC group, we included patients who had AC diagnosis during at least 3 outpatient visits or 1 inpatient admission during 2000 to 2013. The index date was the date of the first AC diagnosis for cases. Controls were assigned the closest index date of hospital visit within 1 month as their matched patient with AC diagnosis. Third, we excluded patients whose gender or urbanization level was unknown or unrecorded, who aged < 20 years. After exclusion, there were 24,414 patients with AC and 923,831 patients without AC. Lastly, we included 24,414 cases and matched them with 97,656 people without AC (1:4 matching) on age, gender, and index date. Figure 1 shows a flow diagram of the selection process.

2.3. Outcomes and covariates

Patients with pre-existing comorbidities of thyroid disorders, diabetes mellitus, hyperlipidemia, hypertension, and rheumatoid arthritis^[10–12] were identified using ICD-9-CM diagnosis codes. We assessed the association between the patients' comorbidities that occurred within 1 year prior to the index date and the risk of AC. These diagnosis codes have been validated in Quan et al's study^[17] and are displayed in Supplemental Table S1, http://links. lww.com/MD/D253.

Pre-existing shoulder diseases and traumatic injuries of the shoulder were defined as individuals who were diagnosed within 1 year prior to the index date. We used ICD-9-CM diagnosis codes to identify patients with shoulder diseases of rotator cuff syndrome, biceps tendinitis, calcific tendinitis, osteoarthritis, and impingement syndrome and patients with fracture, dislocation, or trauma (i.e., sprain, strains, or open wound) on the shoulder (Supplemental Table S1, http://links.lww.com/MD/D253).



Figure 1. Flow chart of the selection process. ICD-9-CM=international Classification of Disease, Ninth Revision, Clinical Modification, LHID Longitudinal Health Insurance Database, NHIRD=National Health Insurance Research Database.

The following covariates included age, gender, urbanization level, and monthly income. We used urbanization and monthly income as a proxy for socioeconomic status. Urbanization level of the individual's employment or residential area was grouped into suburban or rural and urban. Monthly income was determined according to work salary and was grouped into \leq New Taiwan dollars (NTD)\$15,840; 15,841–28,800; 28,801–45,800; and >45,800.

2.4. Statistical analysis

For annual incidence during 2000 to 2013, the numerator is the number of newly diagnosed AC cases in the indicated year and the denominator is the total number of subjects who were alive with and without diagnosis of AC in the indicated year.^[18] Each AC case was counted only once. For annual prevalence, the numerator is the number of patients with AC in the indicated year and the denominator is the total number of the population at risk in the indicated year. The age-specific and gender-specific annual incidence and prevalence rates of AC were calculated for age groups (\leq 40, 40–49, 50–59, 60–69, and \geq 70 years) and genders. In addition, the annual age-gender standardized incidence and prevalence rates of AC for age groups and genders were estimated using the World Health Organization's 2000 to 2025 world standard population age structure.^[19]

Basic characteristics between matched cases and controls were examined using chi-square or Fisher exact tests. Univariable and multivariable logistic regression models with odds ratios (OR) and 95% confidence intervals (CI) were used to identify the relationship between pre-existing shoulder diseases and traumatic injuries of the shoulder and the development of AC. All tests were 2-tailed and *P* values < .05 were considered statistically significant. All analyses were conducted using SAS software, version 9.4 (SAS Institute, Cary, NC).

3. Results

The total number of newly diagnosed AC cases ranged from 1433 to 2040 patients per year (Supplemental Table S2, http://links. lww.com/MD/D253). The annual incidence of AC was the highest in 2004 (22.4 per 10,000 person-years) and the lowest in 2013 (17 per 10,000 person-years). The annual incidence was higher in females (20.5-28.7 per 10,000 person-years) than in males (13.6-16.9 per 10,000 person-years). The annual agegender standardized incidence remained higher in females (13.9-26 per 10,000 person-years) than in males (9.7-15.7 per 10,000 person-years) (Supplemental Table S2, http://links.lww.com/ MD/D253). In addition, the annual age-specific incidence of AC was the highest among patients aged 60 to 69 years (42.5-78.5 per 10,000 person-years) and the lowest among those aged < 40 years (1.4-2.2 per 10,000 person-years) (Supplemental Table S3, http://links.lww.com/MD/D253). However, the annual age-gender standardized incidence was highest among patients aged 50 to 59 years (3.7-6.4 per 10,000 person-years) and lowest among those aged < 40 years (1–1.6 per 10,000 person-years).

The annual prevalence of AC increased from 19.6 to 264.3 per 10,000 persons over 14-year period; annual age-gender standardized prevalence increased from 20.5 to 170.9 per 10,000 persons (Supplemental Table S4, http://links.lww.com/MD/ D253). Females (14.9–199.4 and per 10,000 persons) and patients aged \geq 70 years (72.7–821.8 per 10,000 persons) reported a higher annual prevalence than their counterparts.

 Table 1

 Baseline characteristics in the case and control groups*.

	Case group (n=24,414)	Control group (n=97,656)	P value
Characteristic	n (%)	n (%)	
Age, y			
20–29	305 (1.3)	1220 (1.3)	1.000
30–39	904 (3.7)	3616 (3.7)	
40-49	5000 (20.5)	20,000 (20.5)	
50-59	7992 (32.7)	31,968 (32.7)	
60-69	5502 (22.5)	22,008 (22.5)	
≥70	4711 (19.3)	18,844 (19.3)	
Gender			
Male	9517 (39.0)	38,068 (39.0)	1.000
Female	14,897 (61.0)	59,588 (61.0)	
Urbanization level			
Rural or suburban	8434 (34.6)	37,882 (38.8)	<.001
Urban	15,980 (65.5)	59,774 (61.2)	
Monthly income (NTD)			
≤15,840	7379 (30.2)	31,744 (32.5)	<.001
15,841-28,800	11,589 (47.5)	47,379 (48.5)	
28,801-45,800	3740 (15.3)	13,078 (13.4)	
>45,800	1706 (7.0)	5455 (5.6)	

NTD = new Taiwan dollar, SD = standard deviation.

* Cases and controls were matched in a ratio of 1:4 based on age, gender, and index date.

However, higher age-gender standardized prevalence rates were observed in females and those aged 50 to 69 years (Supplemental Table S5, http://links.lww.com/MD/D253).

Table 1 shows the characteristics of 24,414 cases and 97,656 matched controls. Of patients with AC diagnosis, 53.0% were aged 40 to 59 years and 61.0% were females. Cases and controls were similar in the distribution of age group and gender because of matching. Cases were significantly more likely than controls to live in the urban areas (65.5% vs 61.2%) (Table 1).

Patients with AC were more likely than those without AC to have comorbidites of thyroid disorders (3.1% vs 2.1%), diabetes

(18.2% vs 11.2%), hyperlipidemia (18.6% vs 11.6%), hypertension (32.7% vs 26.2%), and rheumatoid arthritis (0.9% vs 0.5%) (Table 2). Thyroid disorders (OR = 1.34, 95% CI = 1.23–1.46), diabetes (OR = 1.51, 95% CI = 1.44–1.57), hyperlipidemia (OR = 1.42, 95% CI = 1.37–1.49), hypertension (OR = 1.21, 95% CI = 1.17–1.26), and rheumatoid arthritis (OR = 1.54, 95% CI = 1.31–1.82) were significantly associated with subsequent AC after adjusting for age, gender, urbanization level, and monthly income.

Multivariate analyses showed that patients with pre-existing shoulder diseases had significantly higher risk of subsequent AC compared with those without pre-existing shoulder diseases after adjustments. The odds of AC were the highest for calcific tendinitis (OR=8.74, 95% CI=5.66–13.5), followed by biceps tendinitis (OR=7.93, 95% CI=5.33–11.79), rotator cuff syndrome (OR=6, 95% CI=5.26–6.85), osteoarthritis (OR=4.27, 95% CI=3.44-5.3), or impingement syndrome (OR=3.13, 95% CI=2.64-3.71) (Table 2) and were illustrated in Supplemental Figure S1, http://links.lww.com/MD/D253. In addition, a prior history of fracture was associated with the highest odds ratio of AC (OR=4.51, 95% CI=3.82-5.34), followed by dislocation (OR=3.57, 95% CI=2.35-5.45).

4. Discussion

In this nationwide, population-based study, we found that the annual incidence of AC decreased significantly over the 14-year study period among patients aged 40 years and older. The majority of AC patients were female and aged 50 to 69 years, which were consistent with the previous data.^[5,20] The decreasing trend of the annual incidence in Taiwan may be due to increased numbers of patients receiving care and treatment. The incidence of AC in our study is much lower than the incidence from prior studies.^[10,20] One possible reason for the discrepancy could be that some incidence studies evaluated patients with specific comorbid conditions with a higher incidence of AC than the general population.^[20] The

Table 2

Univariate and multivariate logistic regression analyses of pre-existing comorbidites, shoulder diseases, and traumatic injuries of the shoulder associated with subsequent adhesive capsulitis.

Variable	Cases (n=24,414) n (%)	Controls (n=97,656) n (%)	COR (95% CI)	AOR (95% CI)	P value for AOR
Thyroid disorders	756 (3.1)	2044 (2.1)	1.50 (1.37-1.63)	1.34 (1.23-1.46)	<.001
Diabetes mellitus	4434 (18.2)	10,900 (11.2)	1.77 (1.70-1.84)	1.51 (1.44-1.57)	<.001
Hyperlipidemia	4545 (18.6)	11,299 (11.6)	1.75 (1.68–1.82)	1.42 (1.37-1.49)	<.001
Hypertension	7989 (32.7)	25,596 (26.2)	1.37 (1.33-1.41)	1.21 (1.17-1.26)	<.001
Rheumatoid arthritis	213 (0.9)	524 (0.5)	1.63 (1.39-1.92)	1.54 (1.31-1.82)	<.001
Shoulder disease [†]					
Calcific tendinitis	94 (0.4)	29 (0.03)	13.01 (8.57–19.73)	8.74 (5.66-13.50)	<.001
Biceps tendinitis	99 (0.4)	37 (0.04)	10.74 (7.36-15.67)	7.93 (5.33–11.79)	<.001
Rotator cuff syndrome	670 (2.7)	374 (0.4)	7.34 (6.46-8.34)	6.00 (5.26-6.85)	<.001
Osteoarthritis	222 (0.9)	158 (0.2)	5.66 (4.61-6.94)	4.27 (3.44-5.30)	<.001
Impingement syndrome	293 (1.2)	306 (0.3)	3.86 (3.29-4.54)	3.13 (2.64-3.71)	<.001
Traumatic injuries of the shoulde	er [†]				
Fracture	338 (1.4)	263 (0.3)	5.20 (4.42-6.11)	4.51 (3.82-5.34)	<.001
Dislocation	63 (0.3)	42 (0.04)	6.01 (4.06-8.88)	3.57 (2.35-5.45)	<.001
Trauma	29 (0.1)	63 (0.06)	1.85 (1.19–2.87)	1.43 (0.90-2.26)	.133

AOR = adjusted odds ratio, CI = confidence interval, COR = crude odds ratio.

* The model was adjusted for age, gender, urbanization level, and monthly income.

[†] The model was adjusted for age, gender, urbanization level, monthly income, and comorbidites.

incidence of AC in diabetic patients is reported to be 10% to 36%,^[21] which would be an overestimation for general population. Another possible reason could be that prior studies included both AC and other shoulder impairment.

Women had higher incidence and prevalence rates of AC than man, possibly due to the fact that thyroid disorders and calcified tendinitis are more frequently in women while diabetes is more frequently encountered in men.^[22] In our study, these 2 conditions are associated with AC development. Thyroid disorders have been reported to increase the risk of AC in prior studies.^[2,13] However, clinical evidence suggested that thyroid disorder may play a role in the pathogenesis of calcified tendinitis,^[22] which could in turn contribute to the higher incidence and prevalence of AC in women.

Our results indicated that comorbidities of thyroid disorders, diabetes, hyperlipidemia, hypertension, and rheumatoid arthritis were significantly associated with the development of AC, which are consistent with previous studies.^[2,11–14,23] Two populationbased cohort studies from Taiwan found that patients with diabetes or hyperthyroidism had 32.1%^[10] and 22%,^[2] respectively, higher risk of developing AC, as compared with their counterparts. Similarly, hyper-cholesterolemia and inflammatory lipoproteinemias significantly correlated with primary AC were found in univariate analyses.^[23] In addition, 1 casecontrol study in Brazil reported that hypothyroidism diagnosis was more likely to present in AC patients than in their counterparts.^[13] Schiefer et al^[13] suggested that higher serum thyroid-stimulating hormone levels were observed among patients with bilateral and severe conditions of AC than in those with unilateral AC. Patients with concomitant systemic diseases such as thyroid function disorder, diabetes, and rheumatoid arthritis may exacerbate their potential to cause AC. Thus, it should be mentioned that patients with severe comorbid conditions may have higher risk for developing AC.

Furthermore, our results are partially consistent with previous studies^[12,24] that found a history of shoulder trauma, partial-, and full-thickness tear of the rotator cuff correlated with AC. We further revealed that individuals with pre-existing calcific tendinitis, biceps tendinitis, rotator cuff syndrome, osteoarthritis, impingement syndrome, fracture, and dislocation of the shoulder had significantly increased risk of subsequent AC after adjustments. This may be because involvement of supraspinatus tendinitis, rotator cuff syndrome, osteoarthritis, and bone fractures may be associated with long-term consequences of impaired function of the shoulder.^[25] In addition, progressive damage to the shoulder joint and capsule,^[5] humeral fracture, and dislocation^[26] may be present in severe forms of AC. Of note, osteoarthritis and AC were distinct entities with similar exam findings that could easily be distinguished with radiographs; however, osteoarthritis was observed as a risk factor for the development of AC. Therefore, early appropriate management of pre-existing shoulder diseases and traumatic injuries of the shoulder are necessary to prevent AC and adverse outcomes.

The strengths of this study include the large number of cases to evaluate various types of shoulder diseases and traumatic injuries of the shoulder related to subsequent AC. Patients with calcified tendinitis had the greatest odds of developing AC within 1 year, followed by bicep tendinitis, rotator cuff syndrome, fracture, osteoarthritis, dislocation, and impingement syndrome. Our findings might help orthopedic physicians to recognize the odds of developing AC when patients have pre-existing shoulder diseases. In addition, an appropriately designed nested case-control study within a cohort is universally recognized to yield meaningful findings.

Our study has a few limitations due to the nature of administrative data and observational study. First, resolving of the calcification in calcific tendinitis can induce chemical bursitis with signs which are very similar to signs of AC. In addition, the symptoms for both rheumatoid arthritis and osteoarthritis are different yet very similar. These conditions could potentially lead to a misdiagnosis. However, in addition to the use of ICD-9-CM diagnosis codes for identifying either primary or secondary AC, further evaluations of the radiographs are essential to exclude other diagnoses that could present similar characteristics. Second, our study could have underestimated the incidence of AC because we could assess only the AC patients who sought for medical care and whose condition was correctly coded as AC, who are likely to be patients with moderate to severe AC. Some patients with mild AC might not seek for medical care or might have sought for care but were not coded as AC, and thus, might have been omitted in our study. Third, side-specific (i.e., left or right shoulder) data are not available. We could not distinguish if the shoulder disease and AC affected the same side of shoulder, which may underestimate the difference between the 2 groups.

5. Conclusions

This study revealed that in addition to comorbidities, patients with pre-existing calcified tendinitis, bicep tendinitis, rotator cuff syndrome, osteoarthritis, or impingement syndrome, as well as fracture and dislocation, were significantly associated with subsequent AC. These findings suggest that clinicians need to remain aware of pre-existing shoulder diseases and traumatic injuries of the shoulder associated with the development of subsequent AC in the adult population.

Author contributions

Conceptualization: Chung-Yuh Tzeng, Hsiu-Yin Chiang, Ching-Heng Lin.

Data curation: Ching-Heng Lin.

Formal analysis: Hsiu-Yin Chiang, Wei-Szu Lin.

Funding acquisition: Chung-Yuh Tzeng, Ching-Heng Lin.

Methodology: Hsiu-Yin Chiang.

Supervision: Ching-Heng Lin.

- Validation: Hsiu-Yin Chiang, Chun-Che Huang, Ching-Heng Lin.
- Writing original draft: Chung-Yuh Tzeng, Hsiu-Yin Chiang.
- Writing review & editing: Chun-Che Huang, Tzu-Hung Hsiao, Ching-Heng Lin.

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