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Publication Ethics

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Greater Mekong Subregion Medical Journal presents articles in the field of basic and advanced clinical research in medicine and related health sciences, medical education as well as community medicine in Thailand and international, especially in countries of Greater Mekong Subregion.

The journal publishes 3 issues a year: Issue 1 (January - April), Issue 2 (May - August) and Issue 3 (September -December). All submitted research articles and review articles will be evaluated by a single blinded peer-review process and reviewed by 2 experts who have knowledge, expertise, and experience in the field of medicine and related health sciences prior to publication. The journal encloses the information of authors and reviewers. In case of a difference of evaluation, the article evaluation will be considered and given a final decision.

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Original Article

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Greater Mekong Subregion Medical Journal

Prognosis Factors for In-hospital Mortality in Spontaneous Intracerebral Hemorrhage

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Abstract:

Background: Spontaneous intracerebral hemorrhage has the highest mortality of cerebrovascular disease. Previous studies have examined factors contributing to death using binary outcomes but have not analyzed time to death.

Objective: To study prognostic factors for in-hospital mortality in spontaneous intracerebral hemorrhage.

Method: This retrospective cohort design of prognostic research included patients with spontaneous intracerebral hemorrhage from January 2018 to January 2023. Study variable factor and follow time to death refer to the number of days from diagnosis until death within 90 days of hospitalization. Statistical analysis included proportional hazard (PH assumption), then univariable and multivariable Cox's PH regression analysis; results were presented using the Hazard Ratio, 95% CI, p-value < 0.05, and Kaplan-Meier survival curve.

Results: 799 patients were eligible during the period; 153 patients were excluded, and 646 patients were included in the analysis. The mortality rate was 20.7%. Most of the patients were male, with an average age of 60. Multivariable analyses demonstrated that the prognostic factors of mortality included the Glasgow Coma Scale ≤ 8. [mHR 6.33 (95% CI 3.86-10.37), p < 0.001], intraventricular hemorrhage [mHR 5.31 (95% CI 2.94-9.58), p < 0.001], infratentorial location [mHR 2.73 (95% CI 1.51-4.94), p = 0.001], midline shift ≥ 5mm [mHR 2.08 (95% CI 1.04-4.16 p = 0.038], stroke in the young (age ≤ 45 years) [mHR 2.21 (95% CI 1.40-3.47), p = 0.001] and male sex [mHR 1.86 (95% CI 1.25-2.77), p = 0.002]. The prognostic factor for decreased mortality included surgery [mHR 0.25 (95% CI 0.15-0.41), p < 0.001] and door to target SBP in 1 hour [mHR 0.62 (95% CI 0.41-0.93), p = 0.020]. 138 (21.4%) patients underwent a neurosurgical intervention; 106 (76.8%) patients among the survivors compared with 32 (23.2 %) patients who died. Independent predictors of mortality included intraventricular hemorrhage [mHR 6.31 (95% CI 1.49-26.83), p = 0.013] and midline shift > 10 mm [mHR 4.25 (95% CI 1.17-15.39 p = 0.027]

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Conclusion: Glasgow Coma Scale ≤ 8, intraventricular hemorrhage, infratentorial location, midline shift ≥ 5 mm, stroke in the young (age ≤ 45 years), and male sex were significant predictors of in-hospital mortality in a spontaneous intracerebral hemorrhage, whereas surgical therapy and reducing blood pressure to target within 1 hour decreased the in-hospital mortality. Intraventricular hemorrhage and midline shift > 10 mm were predictors of in-hospital mortality in patients who underwent neurosurgical intervention. To reduce death, management for spontaneous intracerebral hemorrhage cases needed to focus on targeting these factors.

Keywords: Prognostic factors, Intracerebral hemorrhage, In-hospital mortality

Introduction

Cerebrovascular diseases remain a significant burden in Thai healthcare; they are the second leading cause of death after cancer.[1] The incidence of intracerebral hemorrhage accounts for 20% of cerebrovascular diseases.[2] Spontaneous intracerebral hemorrhage (SICH) has the highest 30-day mortality rate of cerebrovascular diseases at 30-40%.[3,4] In Thailand, hemorrhagic stroke was associated with the highest estimated mean annual costs, which could be because hemorrhagic strokes are associated with a poorer prognosis and require more resources, such as more extended hospitalizations.[5,6] Death in the hospital after a stroke probably reflects the interface of challenges in optimizing the overall health system. Stroke care teams should effectively estimate prognosis.[7]

Hematoma volume, lower Glasgow Coma Scale (GCS) on admission, and medical comorbidities were critical factors in determining mortality and a poorer prognosis.[4,8] The ICH score is a prognostic model for mortality; it is a simple clinical grading scale that allows risk stratification on presentation with SICH and incorporates measures of symptom severity, age, hematoma volume, hematoma location, and intraventricular hemorrhage (IVH).[9] However, this model only accounts for disease severity factors that cannot be modified. Ignoring treatments in the prognostic model may lead to care limitations in cases with severe initial symptoms, perhaps inappropriately.

SICH causes cerebral tissue damage through two mechanisms. The first mechanism is the direct pressure effect, which can be treated with antihypertensive medications in the acute phase. Antihypertensives are safe and can reduce hematoma expansion in mild to moderate severity patients. The second mechanism comes from the secondary physiologic and cellular pathways. Surgical treatment reduces direct pressure effects and secondary physiologic and cellular pathway damage.

Nonetheless, the benefits of surgical treatment compared to medical therapy alone are still unclear.[3] Hematoma expansion (HE) also presents a poor prognosis and is the aim of acute blood pressure control.[10] The current recommendations are based on data from the two most extensive trials (Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial [INTERACT2] and Antihypertensive Treatment of Acute Cerebral Hemorrhage II [ATACH-2]) for early intensive blood pressure lowering (EIBPL) after SICH, but also have a knowledge gap and need to better delineate the prognostic significance of the magnitude of blood pressure (BP) reduction during the first few hours.[3] Despite the unclear value of craniotomy in improving overall functional benefit or mortality, limited data suggest that craniotomy for

hematoma evacuation might be considered a lifesaving measure in patients who are deteriorating.[3]

The goal of treating SICH is to reduce mortality rates. Thus, identifying treatable prognostic factors for mortality is beneficial in assessing patients and effective treatment planning. This study aims to study the prognostic factors of in-hospital mortality in patients with SICH.

Materials and method

Study design and population

This study is prognostic research using an exploratory model, with data collection done as a retrospective cohort design. Data collection retrieved the patients with a primary diagnosis of SICH, using the 10th revision of the International Classification of Diseases (ICD-10) codes I61.0-I61.9) and received treatment at Phayao Hospital, Phayao Province, from January 1, 2018 to January 1, 2023. A total of 799 patients with abnormal acute neurological symptoms who underwent a computed tomography scan of the brain (CT brain) were diagnosed with hemorrhagic stroke and were at least 18 years of age were included in the study. One hundred fifty-three patients were excluded from the study, including 1) patients with secondary causes of intracerebral bleeding such as an intracranial aneurysm or subarachnoid hemorrhage, cerebral arteriovenous malformation, cerebral venous sinus thrombosis, tumors, and trauma. (95 patients); 2) patients with an abnormal international normalized ratio (INR) ≥ 1.5 or patients taking warfarin (32 patients); 3) patients with a platelet count of < 100,000/mm^3 (19 patients); 4) patients who do not have a brainstem reflex (3 patients); and 5) patients with incomplete medical records (4 patients). A total of 646 patients were included in the study, as shown in Figure 1.

Patients received care according to guidelines on the management of intracerebral hemorrhage[11,12], under the care of a multidisciplinary team, until death or survival on discharge from the hospital. Variables that may be contributing factors to mortality and were included in the study include 1) sex, 2) age, 3) GCS on arrival to the emergency department (ED), 4) location of hematoma, 5) IVH; 6) volume of hematoma measured using the ABC/2 method; 7) midline shift (MLS), measuring the distance of convexity of the corpus callosum at the level of the foramen of Monro, 8) Depth measured from the cortical surface to the outermost border of the SICH, 9) Achieving the target systolic blood pressure (SBP) of 130-150 mmHg in 1 hour (door-to-target SBP in 1 hour) with antihypertensive medication, either nicardipine or labetalol, 10) surgery or neurosurgical intervention was defined as having an operative neurosurgical procedure with craniotomy or craniectomy with blood clot removal or ventriculostomy with external ventricular drainage per indication for surgical treatment. Indications for surgery include a volume of hematoma ≥30 ml, cerebellum hematoma diameter > 3 cm or volume ≥ 15 ml, MLS ≥ 5 mm, and IVH with obstructive hydrocephalus.[11-14] Operation time is initially from the anesthesia procedure until the closure of the scalp. The decision to undergo surgery also depends on an agreed-upon decision and planning between the surgeon, the patient, and the patient's relatives. Once the patient's clinical condition has stabilized, they undergo rehabilitation and intermediate care until discharge. Time to death, which refers to the number of days from diagnosis until death, was followed, with two types of event status: death or censoring within 90 days of hospitalization. This study has the approval of the ethics committee of Phayao Hospital (COA no. 194, PYHREC no. 10/2566).

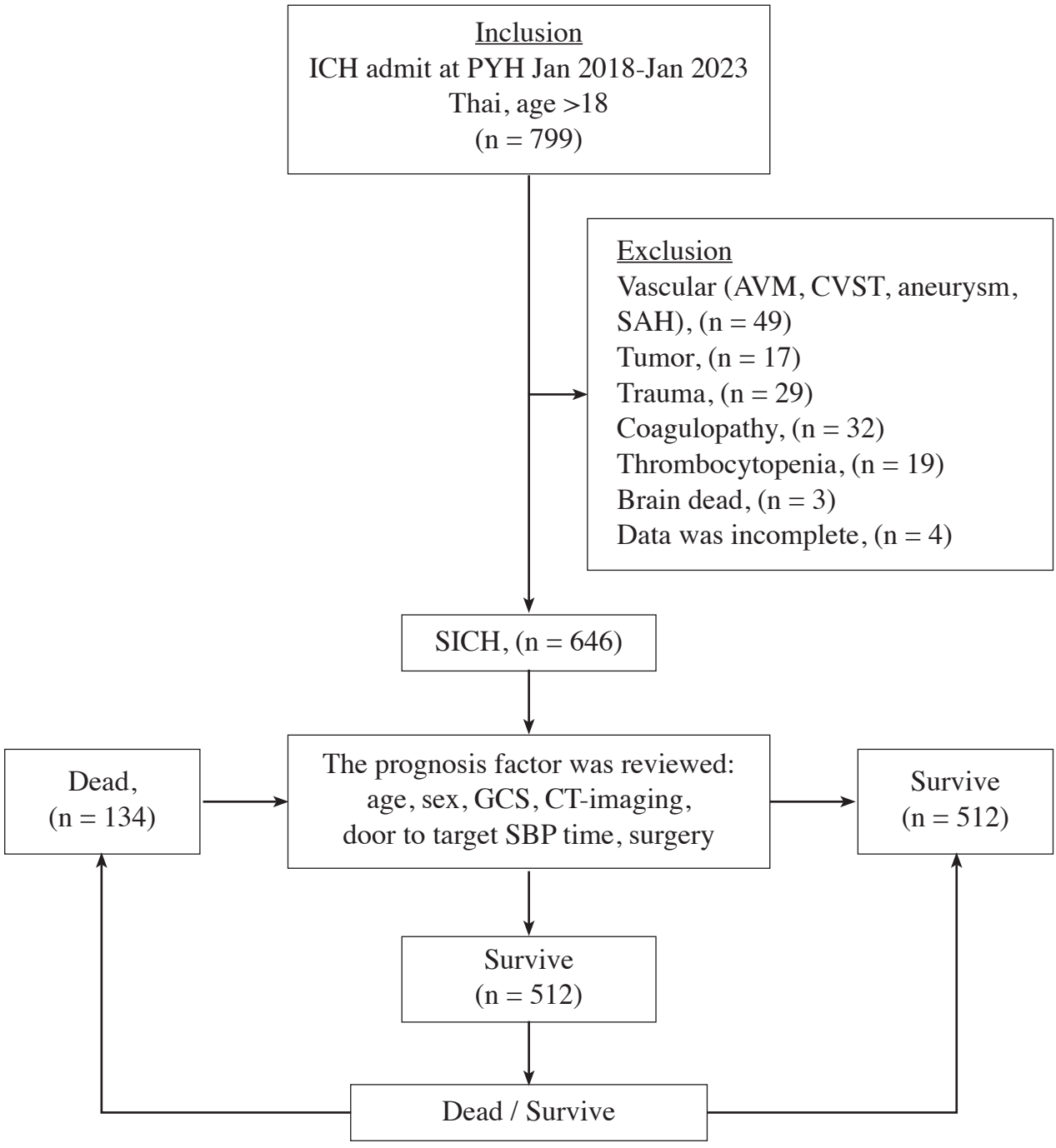

Figure 1 Study flow diagram

Sample size calculation

The sample size was calculated based on a pilot study of 60 cases among patients with SICH at Phayao Hospital. There were 11 cases in the death group and 49 cases in the survival group. Because this study is an exploratory model, it was necessary to calculate the sample size for every predictive factor that was expected to affect death. Calculate sample size using STATA version 18 (licensed) (study size estimation for the Cox proportional hazard model) with alpha error < 5%, power 80%, maximum sample size, and the possibility to collect data, including the variable MLS of ≥ 5 mm, which calculates a hazard ratio equal to 1.68 times, results in the number of death events similar to 117 cases. The pilot study found four times

the proportion of patients who survived to those who died (N2/N1). Therefore, it is necessary to use 117 surviving patients x 4 times = 468 patients, for a total of 585 patients. This sample size can cover factors predicting age ≤ 45 years, GCS ≤ 8, ICH volume, IVH, MLS ≥ 5 mm, door-to-target SBP in 1 hour, and surgery, respectively.

Nonetheless, a larger sample size with more events is a better representation and has better statistical power. As such, the researchers included all patients in the study from January 1, 2018, to January 1, 2023; after exclusion, 646 patients remained.

Statistical analysis

Patients included in all SICHs were divided into two groups: in-hospital deaths and survivors (censoring). Categorical variables were analyzed by Fisher's exact test and assessed as counts and percentages. Continuous variables were analyzed by the Student's t-test or Mann-Whitney U test and considered mean or median with a standard deviation or interquartile range, depending on the data distribution. First, the univariate Cox proportional hazards ratio was used to identify the possible independent risk factors for mortality. The clinically significant variables and all variables with a p-value less than 0.1 were included in the multivariable analysis model. Second, multivariable Cox proportional hazards ratio analysis and the step-backward method were used to identify the independent prognostic factors for mortality. A multicollinearity test was performed. Prognostic factors for decreased mortality were expressed using the Kaplan-Meier survival curve.

Results

This study includes a total of 646 patients with SICH: 134 patients died in the hospital, and 512 patients survived on discharge. The percentage of in-hospital deaths was 20.7, with the majority of patients male, with an average age of 60 years, bleeding in the supratentorial region, a depth > 10 mm, and taking longer than 1 hour to achieve the SBP goal of 130-150 mmHg. In the in-hospital death group, a majority of patients had GCS ≤ 8, and 90% of patients had an IVH, with an average volume of hemorrhage of 38.2 ml (IQR 16.2-91.3 ml) and an average MLS of 5.5 mm (IQR 0–11 mm) (table 1.1). One hundred thirty-eight patients underwent neurosurgical intervention, while 508 underwent conservative treatment. The majority of patients who underwent neurosurgical intervention were male. The average age is about 58 years, and the average GCS is 10.2 ± 3.9. The most bleeding was at the supratentorial location, and the average hematoma volume was 30 ml, with a midline shift of 4 mm (IQR 0–7 mm). 56.5% of patients underwent a craniotomy, 20.3% had a craniectomy, and 23.2% had a ventriculostomy. Thirty-two patients died in the hospital, while 106 survived at discharge. The in-hospital mortality among patients who underwent surgery was 23.2% (table 1.2).

Analysis of prognostic factors for morality was done using a univariable Cox proportional hazard ratio; results showed prognostic factors for increased risk of in-hospital mortality included male sex, stroke in the young (age ≤ 45 years), GCS ≤ 8, infratentorial, IVH, the volume of hematoma > 30 ml, MLS > 5 mm, depth ≤ 10 mm, and prognostic factors for decreased risk of in-hospital mortality included door-to-target SBP in 1 hour and surgery. Subgroup analysis in neurosurgical intervention showed prognostic factors for increased risk of in-hospital mortality included GCS ≤ 8, IVH, volume of hematoma > 60 ml, and MLS > 10 mm (Table 2).

Table 1.1 Characteristics of patients

Clinical characteristics	Death n = 134 (20.7%)	Survival n = 512 (79.3%)	p-value
	n (%)	n (%)	
Gender, n (%)			
Female	35 (26.1)	197 (38.5)	0.008
Male	99 (73.9)	315 (61.5)	
Age (years), mean ± SD.	59.8 ±15.6	62.4 ± 13.2	0.053
> 45	107 (79.8)	458 (89.4)	0.005
≤ 45	27 (20.2)	54 (10.6)	
GCS, mean ± SD	6.6 ±3.8	12.1 ± 3.7	< 0.001
9-15	34 (25.4)	419 (81.8)	< 0.001
3-8	100 (74.6)	93 (18.2)	
Location			
Supratentorial	99 (73.9)	452 (88.3)	< 0.001
Infratentorial	35 (26.1)	60 (11.7)	
Intraventricular hemorrhage	119 (88.8)	203 (39.7)	< 0.001
Volume of hematoma (ml.), median (IQR)	38.2 (16.2, 91.3)	12.3 (5.3, 29.1)	< 0.001
< 30	58 (43.3)	390 (76.2)	< 0.001
30-60	22 (16.4)	71 (13.9)	
> 60	54 (40.3)	51 (9.9)	
Midline shift (mm.), median (IQR)	5.5 (0, 11)	0 (0, 3)	< 0.001
< 5	60 (44.8)	410 (80.1)	< 0.001
5-7	16 (11.9)	46 (9.0)	
8-10	18 (13.4)	16 (3.1)	
> 10	40 (29.9)	40 (7.8)	
Depth (mm.)			
> 10	92 (68.7)	390 (76.1)	0.094
≤ 10	42 (31.3)	122 (23.9)	
Door to target SBP (hour)			
> 1	97 (72.4)	328 (64.1)	0.082
≤ 1	37 (27.6)	184 (35.9)	
Treatment			
Conservative	102 (76.1)	406 (79.3)	0.410
Surgery	32 (23.9)	106 (20.7)	

GCS: Glasgow Coma Scale; SBP: Systolic blood pressure

Table 1.2 Characteristics of patients who had neurosurgical intervention

Clinical characteristics	Death n = 32 (23.2%)	Survival n = 106 (76.8%)	p-value
	n (%)	n (%)	
Gender, n (%)			
Female	10 (31.3)	42 (39.6)	0.415
Male	22 (68.7)	64 (60.4)	
Age (years), mean ± SD	58.5 ± 16.4	58.4 ± 11.8	0.960
> 45	25 (78.1)	91 (85.9)	0.285
≤ 45	7 (21.9)	15 (14.1)	
GCS, mean ± SD	8.6 ± 4.5	10.6 ± 3.6	0.008
9-15	14 (43.7)	73 (68.9)	0.013
3-8	18 (56.3)	33 (31.1)	
Location			
Supratentorial	28 (87.5)	98 (92.5)	0.473
Infratentorial	4 (12.5)	8 (7.5)	
Intraventricular hemorrhage	30 (93.8)	62 (58.5)	< 0.001
Volume of hematoma (ml.), median (IQR)	32.3 (12.2, 75.7)	28.8 (15.9,50.0)	0.247
< 30	15 (46.8)	56 (52.8)	0.129
30-60	6 (18.8)	31 (29.3)	
> 60	11 (34.4)	19 (17.9)	
Midline shift (mm.), median (IQR)	5 (0,11)	3 (0,6)	0.055
< 5	13 (40.6)	67 (63.2)	0.054
5-7	6 (18.8)	18 (17.0)	
8-10	3 (9.4)	7 (6.60)	
> 10	10 (31.2)	14 (13.2)	
Procedure			
Craniotomy	15 (46.9)	63 (59.4)	0.393
Craniectomy	8 (25.0)	20 (18.9)	
Ventriculostomy	9 (28.1)	23 (21.7)	
Operation time (minute), median (IQR)	120 (75,158.5)	107 (80,150)	0.316

GCS: Glasgow Coma Scale; SBP: Systolic blood pressure

Table 2 Univariate Cox's proportional hazard regression analysis

Variables	uHR	95% CI	p-value
Male	1.65	1.12-2.44	0.011
Age ≤ 45 years	1.92	1.25-2.96	0.003
GCS ≤ 8	9.37	6.31-13.92	< 0.001
Infratentorial	2.04	1.37-3.04	< 0.001
Intraventricular	8.36	4.87-14.34	< 0.001
Volume of hematoma (ml.)			
30-60	1.66	1.00-2.74	0.047
> 60	5.01	3.46-7.37	< 0.001
Midline shift (mm.)			
5-7	2.03	1.16-3.54	0.013
8-10	5.22	3.03-8.99	< 0.001
> 10	5.56	3.70-8.37	< 0.001
Depth ≤ 10 mm.	1.46	1.00-2.10	0.047
Door to target SBP in 1 hour	0.71	0.48-1.04	0.075
Surgery	0.62	0.41-0.95	0.030
GCS ≤ 8	2.12	1.04-4.33	0.039
Infratentorial	0.87	0.29-2.59	0.809
Intraventricular	7.15	1.70-30.09	0.007
Volume of hematoma (ml.)			
30-60	0.88	0.34-2.29	0.800
> 60	2.27	1.01-5.10	0.047
Midline shift (mm.)			
5-7	2.07	0.76-5.62	0.152
8-10	2.17	0.28-16.94	0.462
> 10	3.75	1.67-8.43	0.001
Procedure			
Craniotomy	1		
Craniectomy	1.34	0.56-3.23	0.510
Ventriculostomy	1.28	0.55-2.96	0.572
Operation time (minute)	1.00	0.99-1.00	0.512

GCS: Glasgow Coma Scale; SBP: Systolic blood pressure; uHR: Univariable hazard ratio

Multivariable cox proportional hazards ratio analysis was conducted and presented using a multivariable hazard ratio (mHR); results showed prognostic factors for increased in-hospital mortality included GCS ≤ 8 [mHR 6.33 (95% CI 3.86-10.37), p < 0.001], IVH [mHR 5.31 (95% CI 2.94-9.58), p < 0.001], MLS > 10 mm [mHR 3.36 (95% CI 1.58-7.36), p = 0.002], MLS 8-10 mm [mHR 3.75 (95% CI 1.60-8.82), p = 0.002], MLS 5-7 mm [mHR 2.08 (95% CI 1.04-4.16), p = 0.038], infratentorial [mHR 2.73 (95% CI 1.51-4.94), p = 0.001], stroke in the young (age ≤ 45 years) [mHR 2.21 (95% CI 1.40-3.47), p = 0.001], male [mHR 1.86 (95% CI 1.25-2.77), p = 0.002]. The prognostic factor for decreased in-hospital mortality included surgery [mHR 0.25 (95% CI 0.15-0.41), p < 0.001] and door-to-target SBP in 1 hour [mHR 0.62 (95% CI 0.41-0.93), p = 0.020] (table 3). Furthermore, among patients treated with neurosurgical intervention, variables that predicted increased risk of in-hospital death were IVH [mHR 6.31 (95% CI 1.49–26.83), p = 0.013] and MLS >10 mm. [mHR 4.25 (95% CI 1.17–15.39), p = 0.027] (table 3). Prognostic factors for reducing the risk of death were presented using the Kaplan-Meier survival curve (Figure 2 and 3).

Table 3 Multivariable Cox's proportional hazard regression analysis

Variables	mHR	95% CI	p-value
Male	1.86	1.25-2.77	0.002
Age ≤ 45 years	2.21	1.40-3.47	0.001
GCS ≤ 8	6.33	3.86-10.37	< 0.001
Infratentorial	2.73	1.51-4.94	0.001
ICH volume (ml.)			
30-60	0.64	0.36-1.13	0.125
> 60	0.84	0.42-1.66	0.613
Intraventricular	5.31	2.94-9.58	< 0.001
Midline shift (mm.)			
5-7	2.08	1.04-4.16	0.038
8-10	3.75	1.60-8.82	0.002
> 10	3.36	1.58-7.14	0.002
Depth ≤10 mm.	0.95	0.62-1.44	0.799
Door to target SBP in 1 hour	0.62	0.41-0.93	0.020
Surgery	0.25	0.15-0.41	< 0.001
GCS ≤ 8	1.79	0.71-4.50	0.217
ICH volume (ml.)			
30-60	5.00	0.17-1.45	0.201
> 60	0.45	0.11-1.85	0.267

Table 3 Multivariable Cox's proportional hazard regression analysis (cont.)

Variables	mHR	95% CI	p-value
Intraventricular	6.31	1.49-26.83	0.013
Midline shift (mm.)			
5-7	2.25	0.80-6.34	0.125
8-10	2.96	0.35-25.20	0.320
>10	4.25	1.17-15.39	0.027

GCS: Glasgow Coma Scale; SBP: Systolic blood pressure; mHR: Multivariable hazard ratio

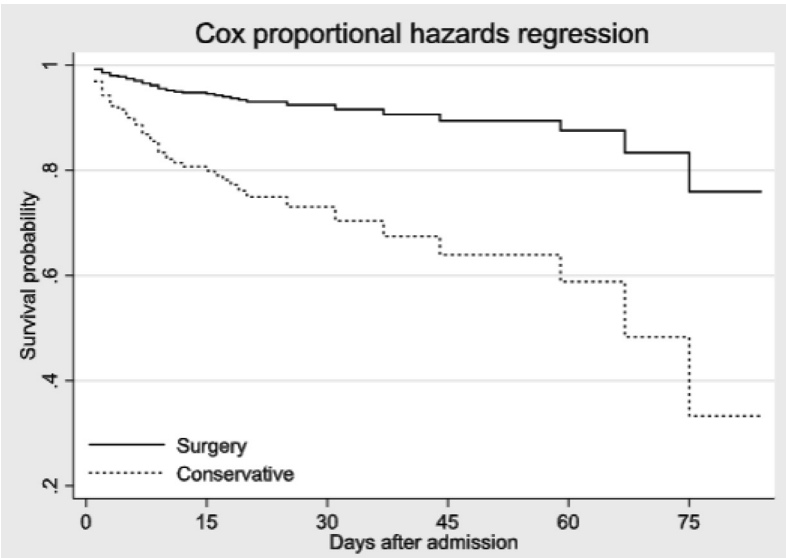

Figure 2 Survival of SICH patients who underwent surgery or conservative treatment

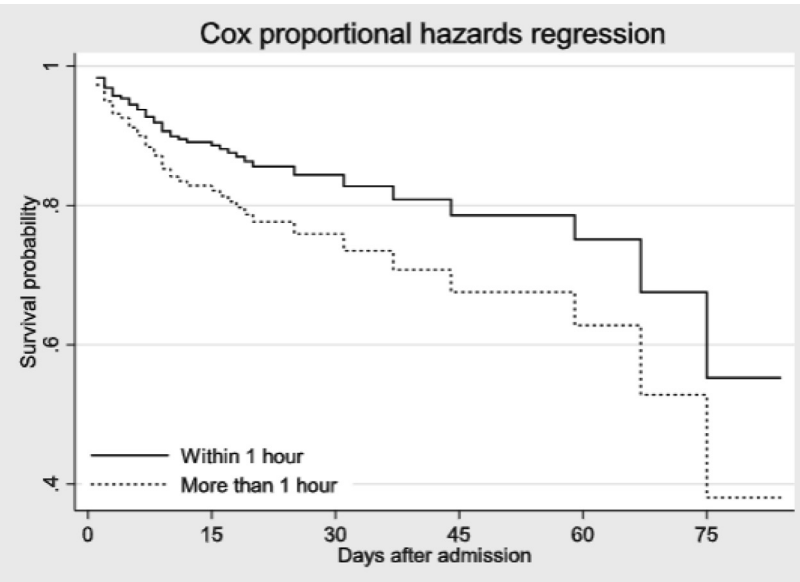

Figure 3 Survival of SICH patients who achieved a target SBP of 130–150 mmHg within or after 1 hour

Discussion

SICH is a life-threatening emergency condition. This retrospective cohort study found that prognostic factors for increased mortality included male sex, stroke in the young (age ≤ 45 years), GCS ≤ 8, IVH, infratentorial location, and MLS ≥ 5 mm; meanwhile, prognostic factors for decreased mortality included the use of intravenous antihypertensive drugs, including nicardipine or labetalol to achieve a target SBP in 1 hour, and surgical treatment.

This study found the in-hospital mortality rate of patients with SICH at 20.7%, lower than a previous study with an in-hospital mortality rate of 24%[15] and a study in Thailand that found it at 26–28%.[16] Nonetheless, this study excluded patients with brain stem death, patients with abnormal INR ≥ 1.5 or patients using warfarin, and patients with a platelet count < 100,000/mm^3 from analysis, which may contribute to a lower mortality rate.

This study reported that men have high mortality; this is in line with previous studies.[17,18] It may be a consequence of behavioral risks such as smoking and alcohol consumption, which contribute to comorbidities such as hypertension, dyslipidemia, and myocardial infarction, contributing to higher mortality compared to women. However, a study by Gokhale et al.[19] found that after adjusting for confounding factors, both sexes have no differences in mortality risk.

We found that patients with stroke in the young (age ≤ 45 years) have a higher mortality risk. However, prior studies have shown that elderly age confers a higher mortality risk[9] can be explained by chronic conditions associated with increased age[20]; as such, old age has a higher mortality risk. Nevertheless, in developing countries, stroke in the young was found to have an increasing mortality risk.[21] A major cause of hemorrhagic stroke in the young is hypertension[22], which has a slower rate of initial diagnosis and poorer control.[23] Furthermore, more youthful age is associated with prolonged hospitalization, which is associated with increased rates of medical complications and worse functional outcomes.[24]

This study found that GCS ≤ 8, IVH, MLS ≥ 5 mm, and infratentorial location were prognostic factors for increased mortality in SICH; this may be because GCS ≤ 8, IVH, and MLS were found to be associated with increased intracranial pressure (ICP), causing decreased cerebral perfusion pressure, consequently leading to poorer treatment outcomes.[25-27]

GCS ≤ 8 was the most vital prognostic factor for in-hospital mortality, similar to the previous study.[28,29] The GCS is a scale widely used to assess the level of consciousness. An earlier occurrence of more consciousness disturbance may, therefore, suggest more significant damage to the involved cerebral structures as well as a greater mortality rate.

IVH causes severe ICP elevations associated with herniation and ischemia. IVH volume and blood breakdown products that promote inflammatory meningitis and hydrocephalus. In the present study, IVH was a prognostic factor for in-hospital mortality. These findings are similar to those of a Qureshi AI et al. study, as hemorrhage volume and ventricular extension are the best predictors of in-hospital mortality.[30] The amount of blood in the ventricles relates directly to the degree of injury and likelihood of survival.[31]

MLS indicates increased intracranial pressure, indicating reduced brain perfusion caused by an intracranial mass or mass effect.[32] Our findings aligned with the previous study[33], which reported that MLS ≥ 5 mm was a prognostic factor for in-hospital mortality.

Infratentorial location, including brain stem or cerebellar hemorrhage, conferred a higher risk of mortality; despite the smaller

volume of hematoma in this area, there is a higher severity, and it is more life-threatening.[34]

This study showed that reducing SBP to 130–150 mmHg within 1 hour after the patient's arrival at the ED helps reduce mortality risk. The findings corresponded to new recommendations for acute BP lowering and recommendations to initiate EIBPL. Initiating treatment within 2 hours of ICH onset and reaching the target within 1 hour.[3] Nevertheless, success in BP reduction to target levels depends on cerebral pathophysiology, or the Cushing reflex, where increased ICP leads to a systemic hypertension response. As such, patients with severe SICH present with higher BP, and reducing BP to target levels is more difficult in this group of patients. A previous study reported that BP reduction decreased HE but did not decrease mortality.[35] However, a prospective study may be required to confirm the importance of various BP measures and the prognostic significance of the magnitude of BP reduction during the first few hours, and the fast-track protocol may play a significant role in controlling the target time.

Theoretically, surgery for blood clot removal confers the benefit of reducing the mass effect and cellular toxicity from residual hemoglobin breakdown. However, a large randomized clinical trial[36] did not find that early surgery has improved treatment outcomes compared to conservative treatment. Nonetheless, there was a crossover from the conservative group to the surgical treatment group if the patients deteriorated. This study found that the in-hospital mortality rate in patients treated with neurosurgical intervention was 23%. It is lower than previous studies that found the in-hospital mortality rate in patients treated with neurosurgical intervention was approximately 30–50%.[36–38] This was a retrospective study, and the selection of patients treated with surgery was based on the joint decision of the neurosurgeon, patients, and patient relatives. Most patients who received neurosurgical intervention corresponding to the indications for surgery had a mean GCS of 10, a volume of hematoma of 30 ml, and an MLS of 4 ml. They almost had IVH and supratentorial lesions. This study found that surgery is a prognostic factor for a decrease in hospital mortality [mHR 0.25 (95% CI 0.15-0.41), $p < 0.001$]. It suggests that neurosurgical intervention in patients with life-threatening conditions helps reduce death in patients with intracerebral hemorrhage. Findings also correspond to the current recommendation[3], which recommended lifesaving surgery in patients with ICH that had deteriorated. A subgroup analysis of patients with intracerebral hemorrhage who received neurosurgical intervention showed that factors predicting in-hospital mortality include GCS ≤ 8, volume of hematoma > 60 ml, IVH, and MLS > 10 mm. During multivariable analysis, it was found that IVH and MLS > 10 mm were predictive factors for in-hospital mortality. Increasing the number of study samples may reveal more correlations among these factors. The current recommends that external ventricular drainage plus thrombolytics is safe and reasonable compared with external ventricular drainage alone to reduce mortality.[3] This retrospective study has not yet used intraventricular thrombolysis in IVH patients; it was a significant predictive factor for death in this study. Decompressive hemicraniectomy may reduce mortality in patients with supratentorial ICH who are in a coma and have large hematomas with midline shifts. The MLS-to-volume ratio showed a significant negative linear correlation with age and higher parenchymal compliance in older individuals due to increased brain atrophy.[39] MLS, which is better than using the hematoma volume alone to represent increased intracranial pressure.

This study found that MLS > 10 mm was a significant prognostic factor for in-hospital mortality. Consideration for decompressive hemicraniectomy in patients with MLS > 10 mm may help reduce mortality in this group of patients. The IVH with intraventricular thrombolysis and MLS > 10 mm with decompressive craniectomy are factors that should be studied further.

This study shows that neurosurgical intervention in patients with intracerebral hemorrhage may help reduce in-hospital mortality in patients with the following factors: GCS > 8, volume of hematoma 30–60 ml, MLS 5–10 mm. However, in patients with IVH, MLS > 10 mm remains an important prognostic factor for hospital mortality in patients undergoing craniotomy, craniectomy, or ventriculostomy.

The limitations of this study included incomplete data as this was a retrospective study. Decisions on surgery, BP control, and supportive care depended on decision-making between the neurosurgeon, patient, and relatives, which may have varied from case to case and may have been influenced by the family's and long-term caretakers' socioeconomic factors. In patients with older age, the family tended to favor conservative treatment despite fulfilling indications for surgery; the family grew to select palliative and supportive care, and cases were transferred to intermediate care facilities.

Conclusion

GCS ≤ 8, IVH, infratentorial location, midline shift ≥ 5 mm, stroke in the young (age ≤ 45 years), and male sex were significant predictors of in-hospital mortality in a spontaneous intracerebral hemorrhage. In contrast, surgical therapy and reducing blood pressure to target within 1 hour may decrease in-hospital mortality. IVH, MLS > 10 mm, remains an important prognostic factor for mortality in patients undergoing surgery. To reduce death, management for spontaneous intracerebral hemorrhage cases needed to focus on targeting these factors.

Conflict of interest

The authors declare they have no conflict of interest related to this research.

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None.

Author contribution

K.C.: concept design, data grouping, data collection, data calculation, data analysis, and manuscript writing;

S.T.: concept design and data collection,

C.K.: data collection.

All authors reviewed this manuscript.

Data sharing statement

The data supporting this study's findings are available from the corresponding author upon reasonable request.

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Special Article

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Treatment of HIV/AIDS with "Dolutegravir-Based Regimen" Antiretroviral Therapy

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Abstract:

Current guidelines recommend dolutegravir (DTG) as the first-line antiretroviral regimen in the treatment of HIV/AIDS. DTG is a second-generation integrase strand transfer inhibitor that has demonstrated high potency, high genetic barrier to resistance, tolerability, minimal drug-drug interactions, and convenience. DTG is also used in a 2-drug regimen among treatment-naive individuals, as well as for switching regimens in virally suppressed HIV/AIDS patients with impaired renal function. However, DTG also has a few considerations. Firstly, DTG has revealed drug-drug interactions with antacids containing aluminum or magnesium, as well as with food or medications containing calcium, iron, or multivitamins, and metformin. Secondly, DTG can increase serum creatinine levels without impacting glomerular filtration rate by inhibiting tubular creatinine secretion. Finally, there was previously a recommendation against using DTG in pregnant women due to concerns about an increased risk of neural tube defects. However, it has been found that the incidence does not differ significantly from the general population. Therefore, almost all current guidelines permit the use of DTG in reproductive-age women and during pregnancy.

Keywords: Dolutegravir, Integrase strand transfer inhibitor, HIV/AIDS

The first report of AIDS patients occurred in 1981 among men who have sex with men (MSM) with *Pneumocystis Carinii* Pneumonia (PCP) in San Francisco and major cities in the United States and Western Europe. The cause of these patients having compromised immunity and being susceptible to opportunistic diseases was initially unknown. It wasn't until 1984 that it was discovered that the low immunity was due to an RNA virus that entered the human body through sexual contact or exposure to infected blood or secretions. This virus destroyed T helper cells, reducing their count from the normal average of 700 cells/mm^3 to below 200 cells/mm^3, which is considered full-blown AIDS. The CD4 T cell count continues to decline until it reaches zero, leaving the immune system weakened and susceptible to various opportunistic infections, ultimately leading to death. Treatment of infected individuals with antiretroviral

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drugs can suppress the virus in the plasma to undetectable levels, resulting in increased immunity and a return to normal quality of life among people living with HIV/AIDS (PLWHA).[1,2]

The evolution of research in developing antiretroviral drugs for HIV has been continuous and accelerated to improve the quality of life for PLWHA. The important classes of antiretroviral drugs are as follows.[3]

1. Nucleoside Reverse Transcriptase Inhibitors (NRTIs): The first drug in this class was Zidovudine (ZVD or AZT), discovered in 1987, followed by Zalcitabine (ddC), Didanosine (ddI), Lamivudine (3TC), Abacavir (ABC), Tenofovir disoproxil fumarate (TDF), and Tenofovir alafenamide (TAF).

2. Protease Inhibitors (PIs): These drugs are used in combination with NRTIs in a regimen known as Highly Active Antiretroviral Therapy (HAART), which began in 1995. HAART can change the course of AIDS from being fatal to having high immunity similar to that of healthy individuals, improving the quality of life. Including Atazanavir (ATV), Ritonavir (RTV), Lopinavir/ritonavir, and Darunavir (DRV).

3. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs): These include Nevirapine (NVP), Efavirenz (EFV), and Rilpivirine (RPV), which have similar efficacy to Protease Inhibitors.

4. Integrase Strand Transfer Inhibitors (INSTIs): This class includes Raltegravir (RAL), Dolutegravir (DTG), Elvitegravir (EVG), and Bictegravir (BIC).

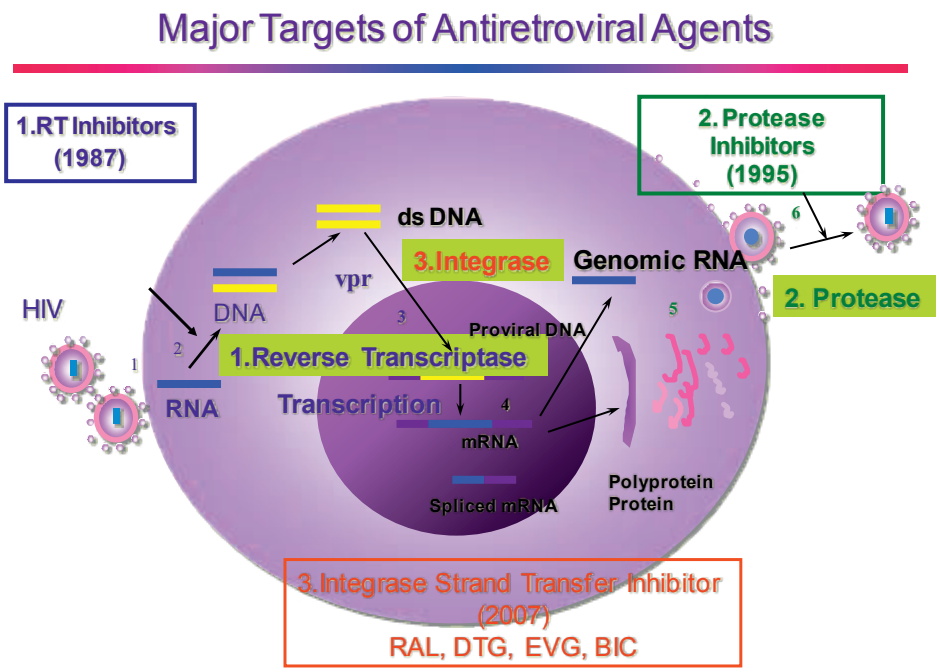

Figure 1 Major Classes of Antiretroviral Therapy

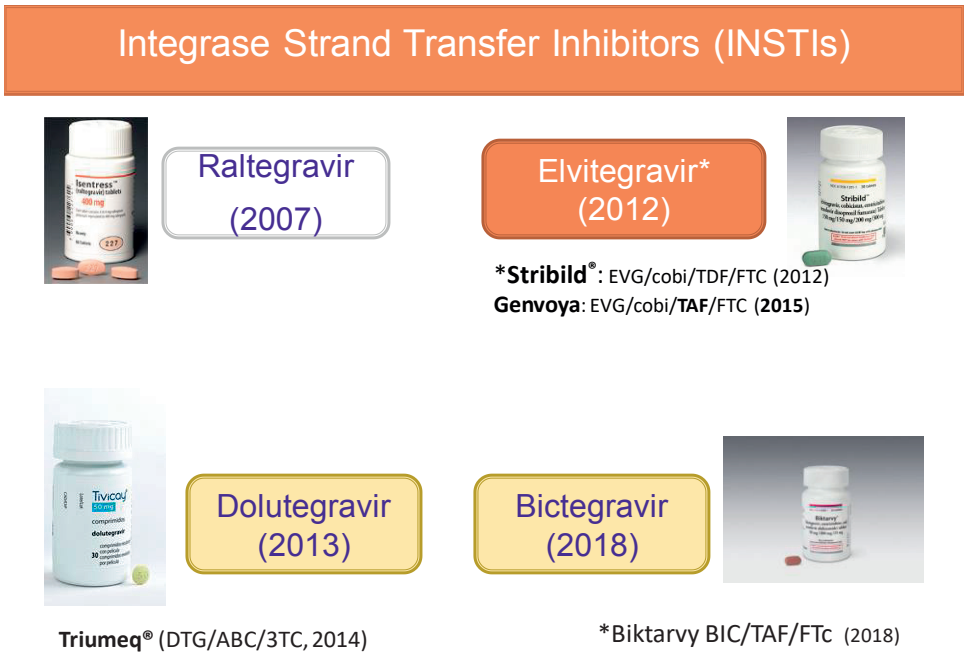

Figure 2 Types of Integrase Strand Transfer Inhibitors

After 2015, international guidelines recommend the use of INSTIs instead of NNRTIs or PIs as the third drug in the first-line drug regimen. INSTIs demonstrated advantages in terms of efficacy, tolerability, less drug interactions, and convenience.

Dolutegravir (DTG) is a second-generation INSTI that has been recommended as a preferred first-line regimen in the current guidelines from the Department of Health and Human Services (DHHS), International AIDS Society (IAS), European AIDS Clinical Society (EACS), and World Health Organization (WHO). This recommendation is based on data showing its high efficacy, high genetic barrier to resistance, and minimal drug interaction.

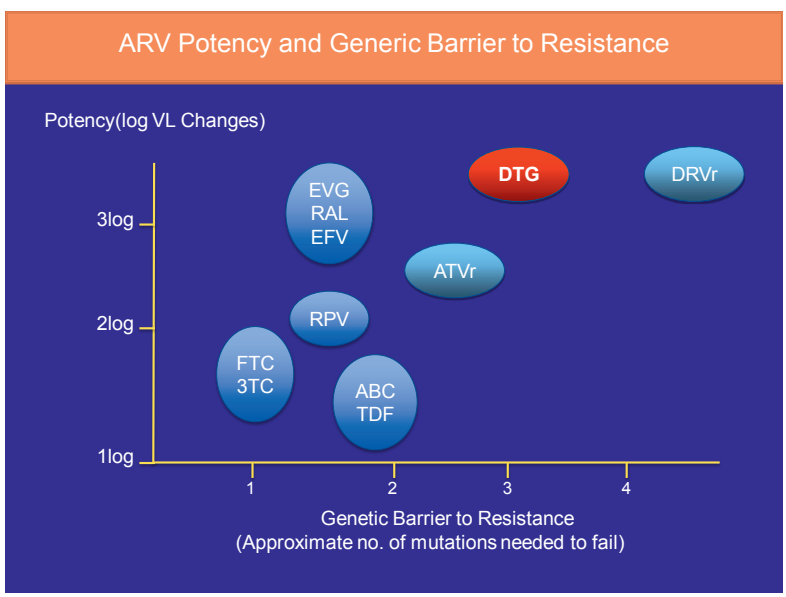

Figure 3 Key Features of Dolutegravir, including its efficacy and high genetic barrier to resistance

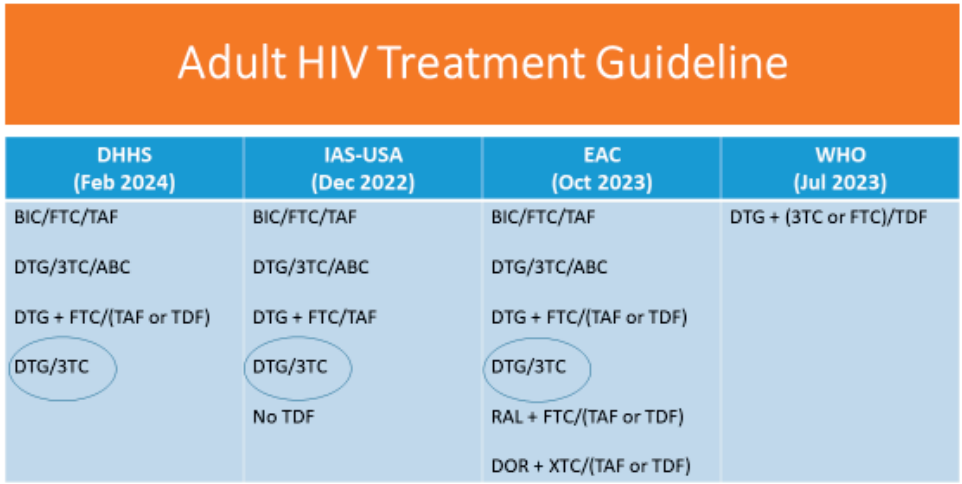

Figure 4 First-line Antiretroviral Therapy according to the 2021-2022 Antiretroviral Therapy Guidelines

Current DHHS Guidelines, Dolutegravir-based regimens are recommended as first-line drugs. Similarly, Thailand's national guidelines also designate Dolutegravir as a preferred first-line drug. Dolutegravir is available in both 50 mg individual tablets and as part of the single tablet regimen TLD (Tenofovir 300 mg, Lamivudine 300 mg, Dolutegravir 50 mg), which is taken as one tablet once daily.

Special considerations for using DTG include:

1. Important Drug-Drug Interactions:

1.1 DTG with antacids containing aluminum or magnesium: DTG can form complexes with Mg^{++} and Al^{+++}, leading to a reduction in DTG levels.[4,5] Studies had shown that DTG should be taken either 2 hours before or 6 hours after antacid intake, to ensure adequate DTG levels.

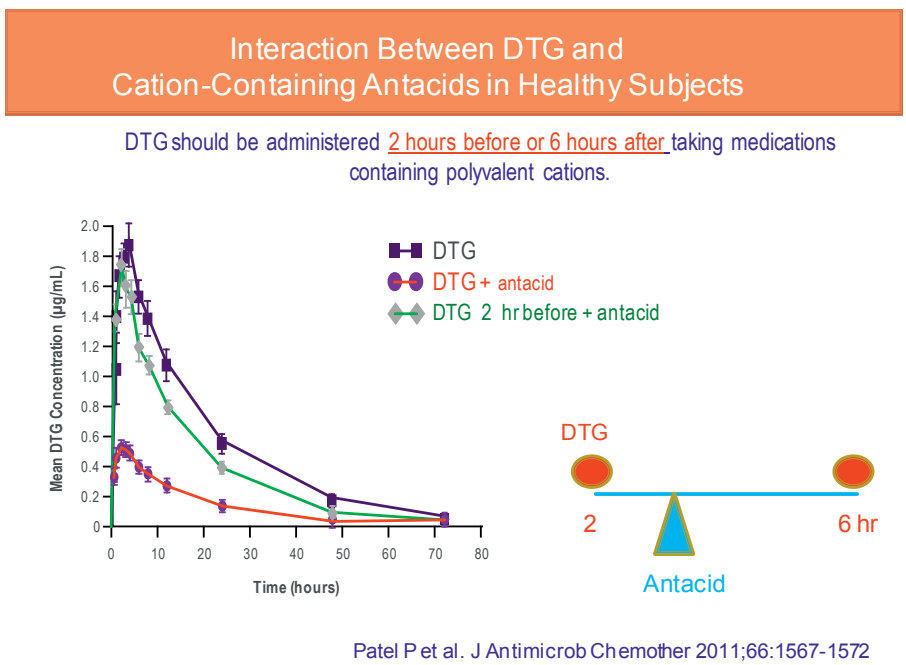

Figure 5 Interaction between DTG and cations in acid-reducing medications

1.2 DTG with food or medications containing calcium, iron, or multivitamins: [4,5] DTG levels in the blood may decrease. To address this, it is recommended to take calcium, iron, or multivitamins along with DTG and with food to ensure sufficient DTG levels for effective viral suppression.

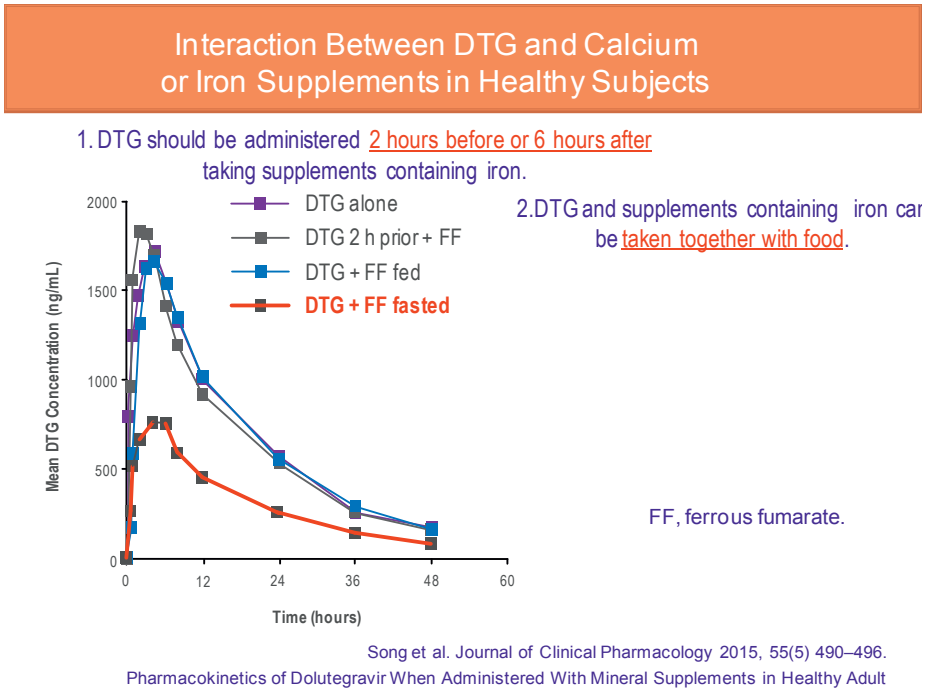

Figure 6 Interaction between DTG and ferrous

1.3 DTG with Metformin:[6,7] Metformin is excreted via the urine through Organic Cation Transporters 2 (OCT2). DTG inhibits the function of OCT2 in the kidneys, leading to reduced excretion of metformin. This results in higher levels of metformin in the plasma. When co-administered, caution is advised due to potential impacts on blood sugar levels, and potential adverse drug reaction of metformin. Consider adjusting metformin dosage to maximal 1 g/day to avoid the risk of lactic acidosis.

Concomitant Drug	Effect on Concentration of DTG	Clinical Comment
metformin	DTG 50 mg. OD Metformin • AUC increases 79% • Cmax increases 66% DTG 50 mg. BID • AUC increases 145% • Cmax increases 111%	• Increase metformin plasma concentration • Consider metformin dose adjustment when starting and stopping DTG

1.4 DTG with antiepileptic drugs:[8]

Phenyltoin is induced by UGT1A1 and CYP3A, which reduces DTG levels. There is no clear study on dosage adjustment. The US guidelines advises against co-administration, while European guidelines recommends adjusting DTG to one tablet twice daily until two weeks after discontinuing antiepileptic drugs.

2. **DTG can increase serum creatinine levels,** particularly in the early initiation because it inhibits the function of Organic Cation Transporter 2 (OCT2), reducing the secretion of creatinine from renal tubular cells, leading to decreased excretion of creatinine into the urine. This can result in a rise in serum creatinine levels by approximately 0.1-0.15 mg/dl for up to 2 weeks after initiation, and these elevated levels may persist for around 48-96 weeks.

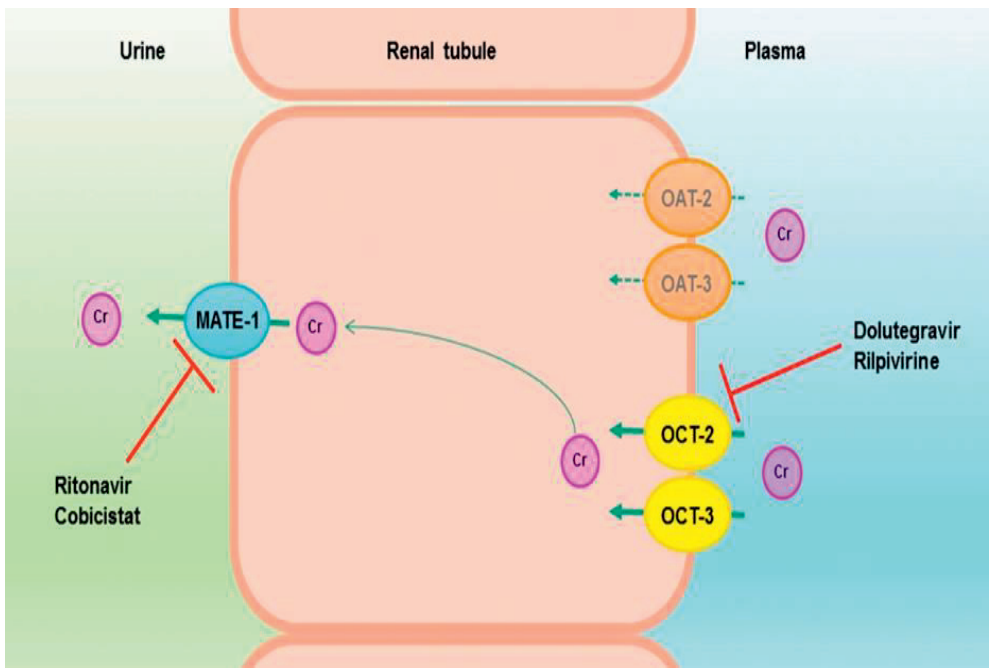

Figure 7 Dolutegravir inhibits the function of Organic Cation Transporter 2, reducing the excretion of creatinine from plasma to urine

3. **DTG adverse reactions:** DTG may interact with various systems, leading to symptoms including[9,10]

Neurological Disorders	
Very common (>1/10)	Headache
Common (<1/10 - >1/100)	Dizziness
Psychiatric Disorders	
Common (<1/10 - >1/100)	Insomnia, anxiety, abnormal dreams, depression
Gastrointestinal Disorders	
Very common (>1/10)	Nausea, diarrhea
Common (<1/10 - >1/100)	Vomiting, flatulence, abdominal pain

4. **The use of DTG during pregnancy:** In early observational studies report an increased incidence of neural tube defects when using DTG during early pregnancy, particularly in the first trimester. Consequently, there was a recommendation against using DTG in pregnant women. However, with more evidence, it was found that the incidence did not differ significantly from the general population. Therefore, after 2019, both DHHS and WHO guidelines permit the use of DTG in reproductive-age women and during pregnancy.[11]

5. **The use of DTG as a first-line 2-drug regimen** has been studied since 2016. GEMINI 1 & 2 studies compared the use of 3TC and DTG in 716 participants, with 3TC, TDF, and DTG in 717 participants, following them for 144 weeks. There were no significant differences in treatment efficacy, viral suppression, and possibly better in reducing TDF-related complications in elderly patients or those with underlying renal dysfunction.[12] Therefore, in 2021, the use of 3TC and DTG as a first-line regimen has been endorsed.

Summary

In 2021, the National AIDS Program in Thailand aligned its antiretroviral therapy guidelines with recommendations from the Department of Disease Control. This resulted in a transition of the first-line drug regimen from 3TC, TDF, EFV to 3TC, TDF, DTG. Moreover, for patients with drug resistance, protease inhibitors have been substituted with INSTIs. Therefore, healthcare professionals, including doctors and nurses, responsible for HIV/AIDS patient care, must possess accurate and comprehensive knowledge of Dolutegravir-based regimens.

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The Processing and Characterization of the New Semi-absorbable Bone Wax Made from Rice Starch Blended with Beeswax

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Abstract:

Background: In the 21st century, bone wax is one of the most prevalent biomaterials to help mechanically control bleeding from bone surfaces in almost every surgical procedure. It is bio-inert, albeit a foreign body with non-absorbability, and rarely causes complications such as granuloma and persistent serous discharge. Semi-absorbable bone wax is an encouraging alternative since it highly reduces the risk of harmful response reactions on the host, which is what we primarily aim for.

Objective: This research studied the amount of medical-grade rice added to beeswax with different amounts of addition. It is used as a semi-absorbable hemostatic agent to improve the biodegradable efficiency of beeswax.

Materials and Method: Material characteristics such as scanning electron microscopy (SEM), melting point, Fourier transform infrared spectroscopy (FTIR), and water diffusibility are used to study the effect of adding rice starch powders. Bone wax is prepared from the mixture of white beeswax with isopropyl palmitate and liquid paraffin and three different compositions of rice starch powders in aqueous suspension (30, 40, and 50 wt %).

Results: The addition of rice starch powder increases the absorbability mechanism, smoothness, and whiteness and can be easily smeared on the bone surface. We have concluded that an optimized composition of 40 wt % rice starch powder has adequate quality for utilizing it as a semi-absorbable bone wax.

Conclusion: Rice starch that is incorporated into bone wax is more bio-absorbable than the original bone wax itself and will furthermore undergo additional testing in animal laboratories.

Keywords: Beeswax, Bone wax, Rice starch, Semi-absorbable, Hemostatic agent

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Introduction

Bone wax is a traditional material used by general surgeons and is used to control massive bleeding from the bone surface during surgery. Bone wax was developed by Horsley in 1892. Its ingredients comprise white beeswax of 7 proportions, almond oil of 1 proportion, and salicylic acid of 1%.[1] Bone wax is sterilized by boiling and preserved in stopper bottles. Parker is the first person to use bone wax.[2] Bone wax consists of white beeswax 80%, liquid paraffin 10% and isopropyl palmitate 10%, which is duplicated from commercial non-absorbable bone wax (Ethicon® Bone Wax, Johnson & Johnson Co., Ltd., US). Although bone wax is effective in controlling bone bleeding. However, the disadvantage of widely used bone wax is non-resorbable. After using bone wax to stop bleeding. Bone wax remains in that location for an indefinite period and may interfere with bone healing and bacteria clearance. This can result in bone infection. Therefore, this research has an idea to develop bone wax with resorbable properties by using fillers obtained from Thai agricultural materials, which are easy to buy and cheap, such as rice, cassava, etc., and medical grade rice starch is used for work in the pharmaceutical industry.

Starch is a polymer that can be completely degraded, and is cheap when compared to other degradable polymer. Pharmaceutical grade purified rice starch powder (Era-Tab®, Erawan Pharmaceutical Research and Laboratory, Co., Ltd, Thailand) (RS) has been used in biomaterial applications.[3] Recently, modified starch has been used as a hemostatic agent due to its water-absorbing properties and when used as a filler in composites. It prevents low molecular weight materials from absorbing blood. It may concentrate platelets and clotting proteins and thereby enhance the external blood clotting mechanism. In this research, we used bone wax as a matrix material. A composite material was prepared from our bone wax and RS with various compositions.

Materials and Methods

Materials

White beeswax (British Pharmacopoeia grade) was purchased from Bronson and, Jacobs International Co., Ltd, Thailand. Liquid paraffin was purchased from S. Tong Chemical Co. Ltd., Thailand. Isopropyl palmitate was purchased from Fluka, Chemika, Switzerland. Era-Tab® (RS) was purchased from Erawan Pharmaceutical Research and Laboratory, Co., Ltd., Thailand.

Samples preparation

Bone wax itself is composed of 80% white beeswax, 10% liquid paraffin, and 10% isopropyl palmitate was prepared through a laminar air flow hood. All composition was weighed with an analytical balance. Then, melt beeswax at 80-100°C for 5 minutes. While the beeswax is melting; blend liquid paraffin and isopropyl palmitate at 60°C for 5 minutes. RS is then added at 30, 40, and 50 wt % as shown in Figure 1. The solution is then stirred for 10 minutes until bone wax is well incorporated with RS. It is then stored and contained in a mold and cooled down to room temperature.

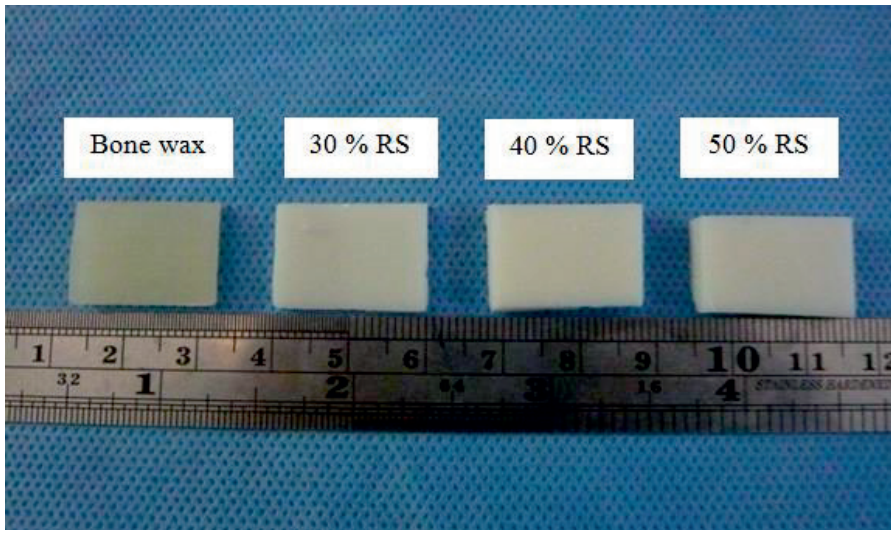

Figure 1 Digital photo of different samples

Characterization

• SEM/EDS

- SEM (JSM-6335F, JEOL, Tokyo, Japan) Energy dispersive spectroscopy (EDS) was used to analyze the morphology of Era-Tab. On the other hand, the light microscope was used to investigate the morphology of the composite surface.

• Thermal analysis

- Thermal analysis was determined by a differential scanning calorimeter (DSC7, Perkin-Elmer). The sample was heated under a nitrogen atmosphere from 20 to 120°C using a scanning rate of 5°C per minute.

• FTIR analysis

- FTIR (FTIR, Thermo Nicolet) was used to characterize the composition and functional group of materials.

• Water diffusibility

- This method was adapted from the equation.[4] Each of the samples was accurately weighed (W1) and separately immersed in distilled water at room temperature for 24 hours. The swollen samples were removed and the excess water was wiped off from the surface. Then, the swollen samples were reweighed (W2). The percent water diffusibility (S) of the samples was calculated using the following equations.

$$S\ (\%) = \frac{(W2-W1)}{W1} \times 100$$

• Statistical analysis of data was collected from three samples that showed average and standard deviation values.

Results and Discussion

This result was found that RS had an average particle size of about 5 to 6 microns (Figure 2). The morphology of the sample surface with 40 wt % of RS showed the particle distribution matrix of bone wax (Figure 3). The chemical compositions of RS powder contained 58.39 ± 1.54 wt % of carbon and 41.61 ± 1.61 wt % of oxygen (Figure 4).

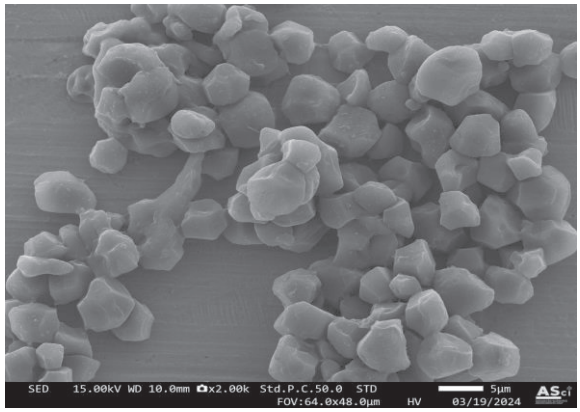

Figure 2 SEM of RS powder

Figure 3 Light micrograph of an additional 40 wt % of RS with magnification of 10X

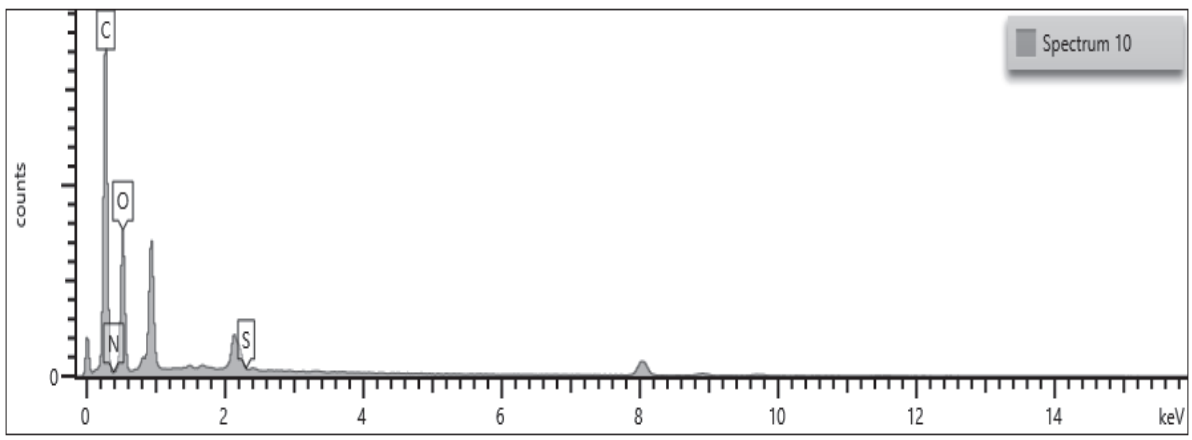

Figure 4 EDS of RS powder

Figure 5 shows the melting point of bone wax increased from 61.52 ± 0.05° C to 63.72 ± 0.04, 64.38 ± 0.05 and 65.52 ± 0.06° C when content of RS increased was 30, 40 and 50 wt %, respectively. This was possibly due to the prevention of starch granules from thermal treatment.

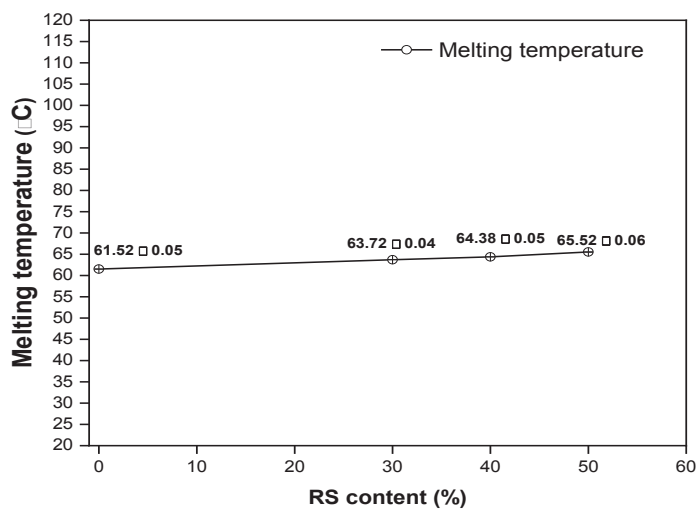

Figure 5 Effect of RS content on the melting temperature of the samples

The FTIR spectra of bone wax, RS, composites are shown in Figure 6, and the most important vibration modes were the C-H stretching around 3000 cm-1 and the -CH deformation modes around 1460 and 1380 cm-1. The atoms directly attached to the aliphatic groups may result in significant shifts from the standard frequencies. In particular adjacent atoms with high electronegativity will shift the band locations to higher frequencies. When two methyl groups were on a single carbon (isopropyl) band of approximately equal intensity, it occurred at near 1390 and 1365 cm-1. The presence of the t-butyl group can be confirmed by the presence of bands around 1255 and 1210 cm-1 while the isopropyl group showed bands near 1170 and 1145 cm-1. When there were four or more CH2 in a row, a rocking absorption was found centered at 720 cm-1. The FTIR spectra of RS showed the prominent peaks at 3300, 2933, 1643, 1156, 1019, 928, and 861 cm-1 which were -OH stretching (3593 to 3643 cm-1), -C-O stretching, and -OH deformation vibration (1050 to 1200 cm-1). The FTIR spectra of the addition RS from 30 to 50 wt % showed that no interaction between bone wax and RS during the physical mixture.

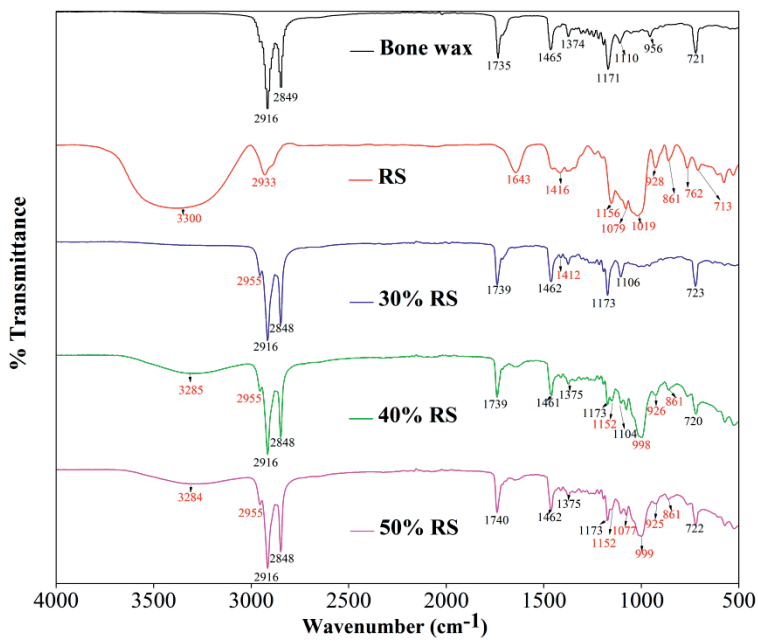

Figure 6 FTIR of bone wax, RS, and different compositions

Figure 7 shows that the water diffusibility of bone wax was constant with an increase in dwelling times due to its non-absorbability. However, RS absorbs water into its structure and swells, thus the addition of RS in the bone wax increased the percentage of diffused water of 30 wt % RS as 0.2 ± 0.22 %, 40 wt % RS as 0.67 ± 0.33 % and 50 wt % RS as 1.47 ± 0.21 % for 80 h. This result showed that 50 wt % of RS in bone wax had the highest percentage of water diffusibility.

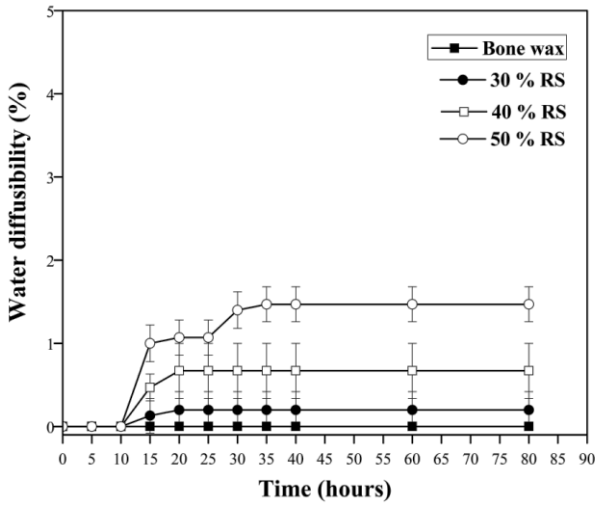

Figure 7 Effect of RS starch content on water diffusibility vs various times

Increasing the content of RS in bone wax increased the melting temperature of the samples due to the obstruction of RS in the bone wax structure. This was possibly due to Era-Tab particles being highly stable and tend to agglomerate. It was used to increase the amount of tablets. There is a wide endothermic temperature range from 70 to 120° C, which may make the melting temperature range of this experiment inconsistent with other studies. The sample that contained RS 40 wt % provides pliability by hand which is similar to commercial bone wax and has potential use as a novel semi-absorbable bone hemostatic wax. However, the effects of water diffusibility of 40 wt % RS are lower than 50 wt % RS due to the amount of RS that is still high on the surface of the bone wax. Water diffusibility of 40 wt % RS has a low percentage because most of the RS content is embedded in a matrix of bone wax. However, commercial bone wax is a bio-inert in the human body. Several studies reported the influence of bone wax on osseous defects. The combination of inhibited osteoblast activities and physical barriers may prevent bone healing and an increased risk of infection.[5] On the other hand, Rockwood, et al[6] implanted bone wax in the bones and muscles of experimental rabbits and they found that the tissue reaction included; 1. No infection 2. Minor absorbability was seen after six months of surgery and inhibition of bone healing, and 3. Minor inflamed reaction on tissue, compared to suture.

Conclusion

A novel semi-absorbable bone wax is softness and pliability to stop bleeding from the bone. The optimized composition was the addition of 40 wt % RS powder into bone wax. Hence the fact that there is more bio-absorbability than the original bone wax and this research should be further tested in animal laboratories.

Acknowledgements

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สำนักวิชาแพทยศาสตร์ มหาวิทยาลัยแม่ฟ้าหลวง
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"Surasi Smart Service" Innovations to Access to Medical History

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The project received the 2024 Invention Innovation Award of "The Military Medical Association of Thailand under the Royal Patronage of His Majesty the King".

Abstract:

Background: Information plays the crucial role in real life. Access to medical history is essential for medical treatments for both patients and medical personnel. Missing an appointment and intermittent treatment leads to worse consequence.

Objective: To ensure that all personnel and service recipients have access to their own health information. To use the same set of health data history. Support the diagnosis and treatment of diseases. To remind patient to come back to see a doctor and reduce waiting time and density in hospital.

Method: Surasi smart service is an innovative invention using Line OA program. After confirming the information, you will be able to view the health check-up results, appointment history, and medication history that you have received. As a result of this innovation, people can view their history even in areas close to hospitals.

Results: The percentage of patients missing appointments decreased from 10.24 % to 2.3%. The percentage of personnel satisfaction with Surasi Smart Service was 93.7%.

Conclusion: The program "Surasi Smart Service" is a program that can increase access to medical services and reduce the rate of missing appointments with eventually increase customer satisfaction.

Keywords: Application, Medical history, Continuity of care

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Introduction

Fort Surasi Hospital is the secondary care unit serving mainly for military personnel and families as well as people around Lardya District area. In the present, personnel affiliated with the army, especially in the 9th Infantry Division, perform continuous missions throughout the year, mostly in remote area and take long period of time. An average of 30 percent of military personnel and their families having chronic disease such as diabetes, hypertension, and dyslipidemia, requires regular medication.

Fort Surasi hospital has the most concern on this issue and initially has developed "Surasi Smart Service" application to lessen the problem. All personnel and health care recipients can easily access to their own health information. Physicians and medical staffs can use the same information of health records to support diagnosis and treatment. The continuous treatment can be easily managed. As well as a real-time service queue notification system to reduce congestion and waiting time in the hospital.

Objective

The project aimed to ensure that all personnel and service recipients can access to their own health information, to use the same data base of health history for supporting medical services in both the diagnosis and treatment of diseases, to remind patients to see a doctor by appointments and to reduce waiting time and density in hospital.

Methods and workflows

Surasi Smart Service is a Web application in the form of Web Service API, bringing the system to be used in the form of Line OA, making it convenient to send messages and various notifications to system users. All personnel and service recipients can access to their own health information. The process starts with scanning the QR code, then filling the ID card number and verifying yourself by entering the last four digits of the hospital. You can find your medical history, including allergy, health appointment, past medication, and also blood test results. There is a recall system for appointments. In case of the results of blood test are abnormal, there is a system to notify the service queue in real time. The special of this program is that users can access to this application either via internet or line OA program. The outstanding feature of this program from those of existing others is a Web application in the form of Web Service API used in the form of Line liff. That benefits to send messages or notifications to users conveniently. All personnel and service recipients can easily access to their own health information including the allergy, previous appointments, medication, vaccination also annual results of physical examination. When the results of the annual physical examination are exceptional, the notification feature shows service queue in real time. The application is user-friendly, it can be accessed anywhere anytime throughout the years via smart phone.

Materials and equipment used in the invention

Hardware aspect: one host computer and one desktop computer

Software aspect: React js, Node js, Line OA and Line Developer Account

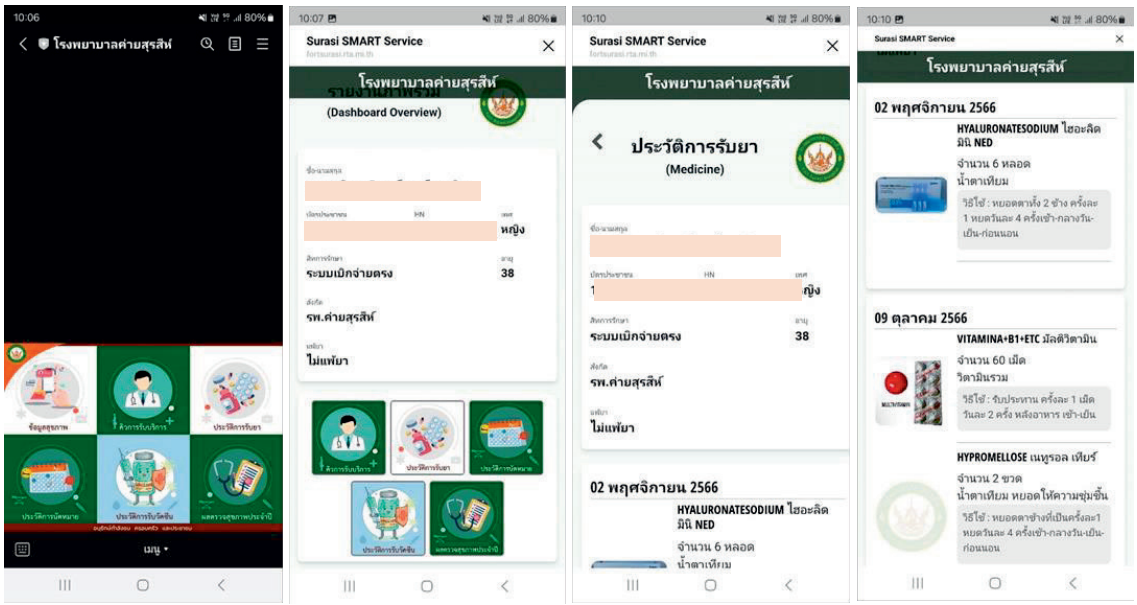

Figure 1 The application can report basic medical history, including allergy, past medication

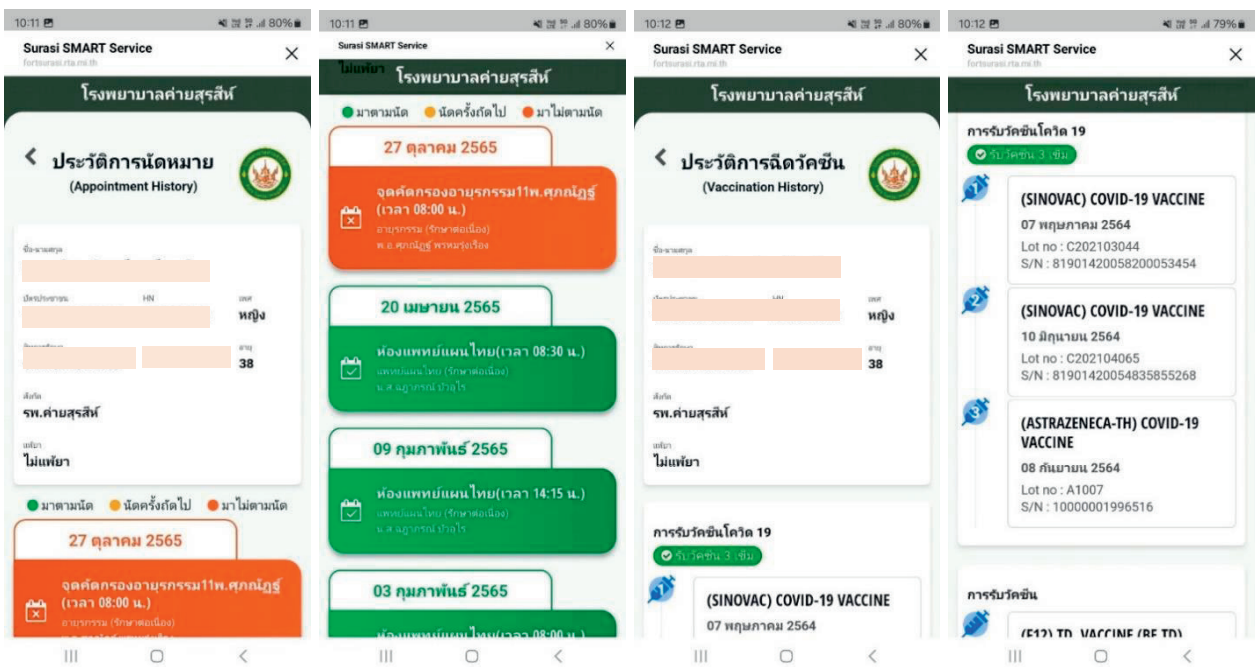

Figure 2 The application can report health appointment, vaccination history

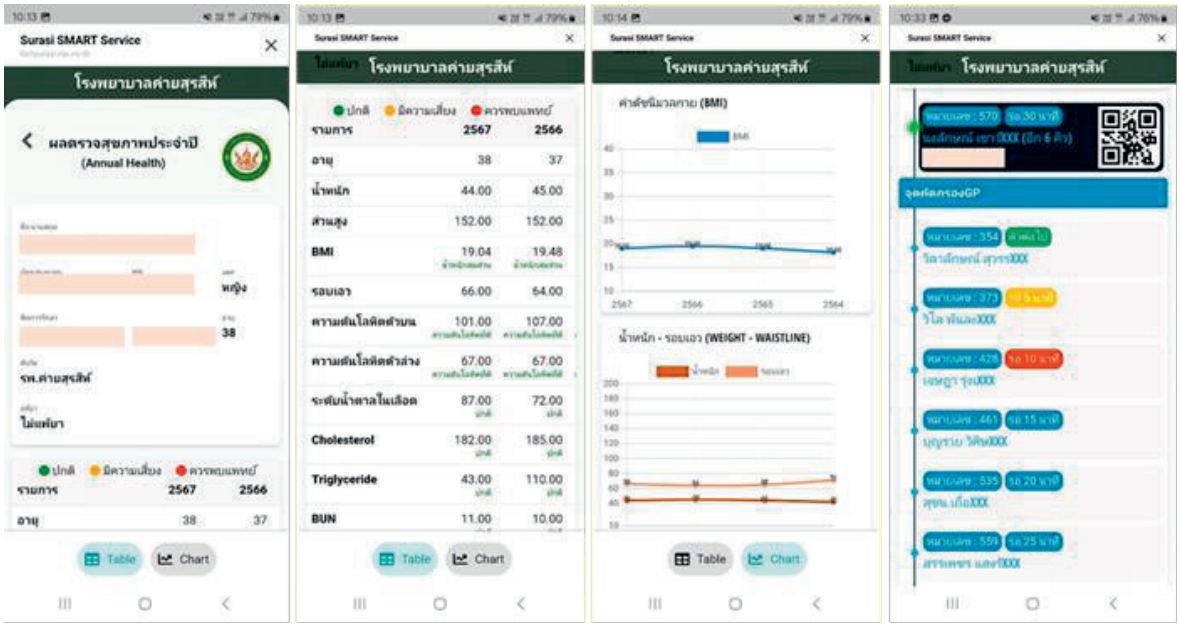

Figure 3 This application can report check-up laboratory and previous laboratory

Result and discussion

Currently, digital technology form Smart phones plays an important role in daily life. People at all levels have access to smart phones and is widely used, whether it is used Smart Phone to communicate through applications.[1] To create a social network (Social Network) or for electronic banking (Internet Banking) etc. through various activities of daily life in our present is almost entirely related to smart phone. All and is not limited to just teenagers or working people. It also includes the elderly. Therefore, these things are reflected the changing way of life in using mobile phone. This is not just a tool for talking or only communication with each other.[2]

As the result of launching Surasi Smart Service Application, all personnel and service recipients approximately 4,682 people have accessed to their own health examination history. The percentage of patients missing the appointments decreased from 10.24% to 2.3%. The percentage of personnel satisfaction with Surasi Smart Service was highly at 93.7%. The Percentage of patient satisfaction with Surasi Smart Service was even higher at 96.1%.

This application won the 2024 Invention Innovation Award of "The Military Medical Association of Thailand under the Royal Patronage of His Majesty the King". It is confirmed that "Surasi Smart Service" is a program that helps to increase the access to medical services and reduce the rate of missing appointments and also increase the customer satisfaction as well.

Acknowledgement

We would like to thank all staffs of Fort Surasi Hospital and the personnel department of the 9th Infantry area for being a part of drivers in the process of developing this program.

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Short Communication GMSMJ Greater Mekong Subregion Medical Journal

Primary Cutaneous Follicle Center Lymphoma Masquerading as Tumid Lupus Erythematosus

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Abstract:

Cutaneous lymphomas, notably indolent cutaneous B-cell lymphoma, can exhibit clinicopathological characteristics resembling those of inflammatory skin conditions. Here, we present the case of an 82-year-old female with recurrent lesions resembling tumid lupus erythematosus on her face. Subsequent histopathological examination and immunohistochemical analysis definitively diagnosed primary cutaneous follicle center lymphoma. This report highlights a rare instance underscoring the importance of considering cutaneous lymphoma as part of the differential diagnosis in patients presenting with inflammatory skin lesions.

Keywords: Primary cutaneous follicle center lymphoma (PCFCL), Tumid lupus erythematosus

Introduction

Primary cutaneous follicle center lymphoma (PCFCL) represents the predominant form of cutaneous B-cell lymphoma, accounting for approximately 60% of cases. It typically affects middle-aged individuals, with a higher prevalence among men.[1] Clinical presentation commonly includes asymptomatic solitary or occasionally multiple erythematous or violaceous papules, plaques, nodules, or tumors varying in size, predominantly observed on the head, neck, or trunk, and infrequently on the lower extremities.[2] Dissemination to other organs is uncommon, occurring in only 5-10% of cases.[3]

Case presentation

An 82-year-old female presented with reddish bumps on her face seven years ago. A skin biopsy conducted at that time revealed findings consistent with tumid lupus erythematosus. Subsequent investigations revealed an antinuclear antibody (ANA) titer of 1:1280 (homogenous pattern). However, other clinical manifestations and investigations for systemic lupus erythematosus (SLE) were unremarkable. Due to maculopathy observed during ophthalmologic examination, initial treatment comprised topical and intralesional corticosteroids alongside oral azathioprine at a dosage of 50 mg/day. After one year of treatment, the lesions improved and resolved, prompting continued azathioprine therapy at the same dosage.

Three months prior to her recent visit, the patient experienced a recurrence of rashes on her face, with an increase in their number. No systemic symptoms were reported. Clinical examination revealed multiple

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ill-defined, discrete, painless erythematous papules and plaques on both cheeks and forehead (Figure 1A-B). Neither hepatosplenomegaly nor lymphadenopathy was detected. Subsequent skin biopsy revealed nodular infiltrations in the dermis consisting of mononuclear cells, displaying a follicular growth pattern. The germinal center areas exhibited a mixture of centroblasts and centrocytes surrounded by reactive lymphocytes (Figure 2A-C). Immunohistochemical staining demonstrated positivity for CD10, CD20, BCL6, and Ki-67 (10-20% of tumor cells), while CD3 and BCL2 were negative (Figure 3).

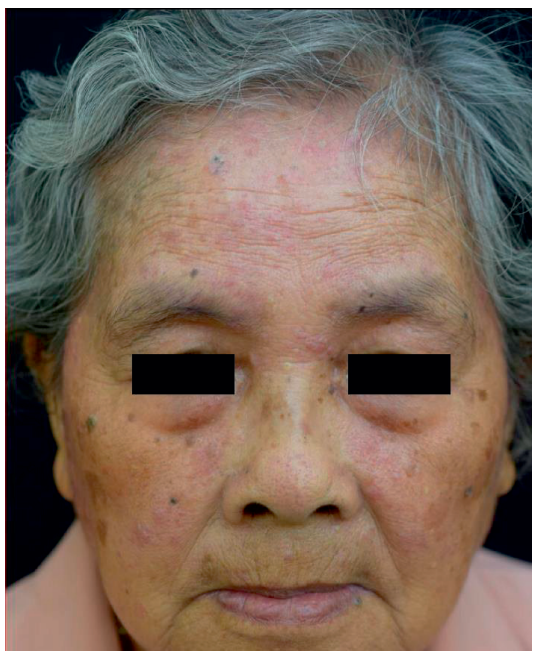

Figure 1A Multiple ill-defined, discrete, painless erythematous papules and plaques on both cheeks and forehead

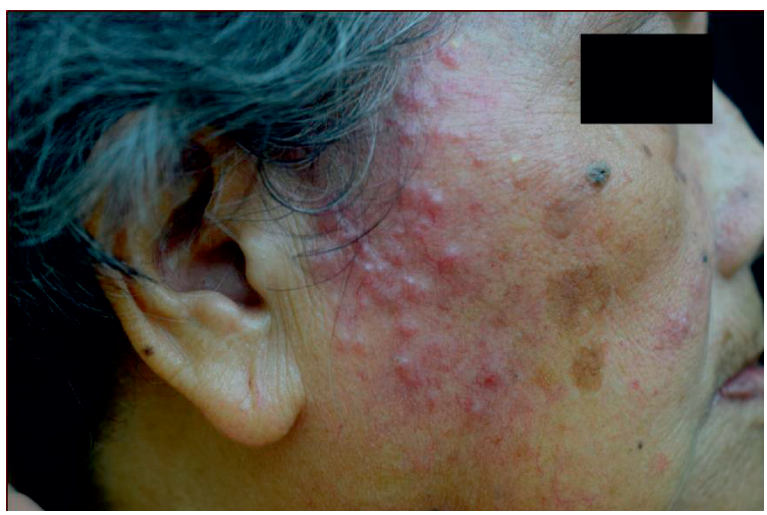

Figure 1B Multiple ill-defined, discrete, painless erythematous papules and plaques on both cheeks

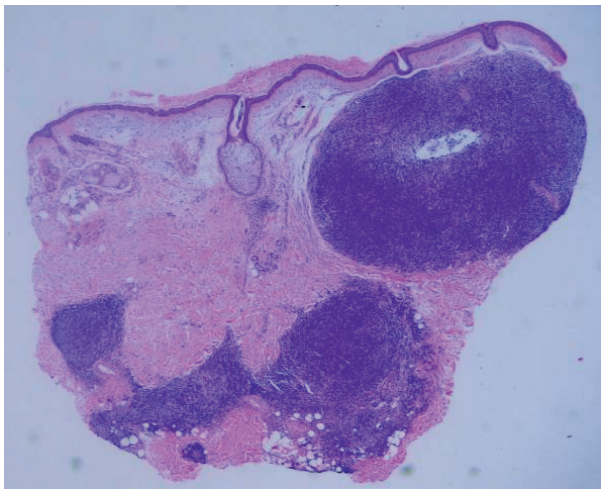

Figure 2A Multiple dense nodular infiltrations in the dermis

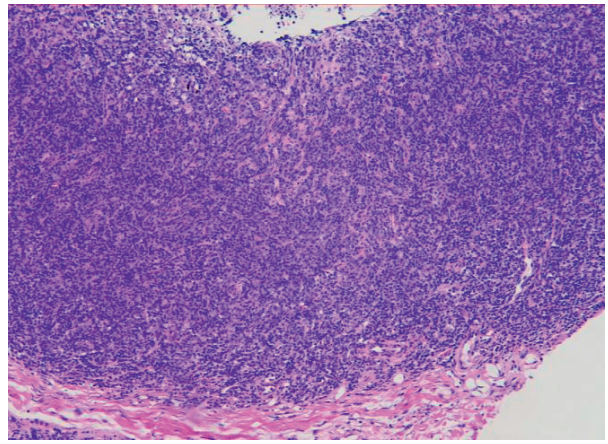

Figure 2B The germinal center areas exhibit atypical mononuclear cells surrounded by reactive lymphocytes

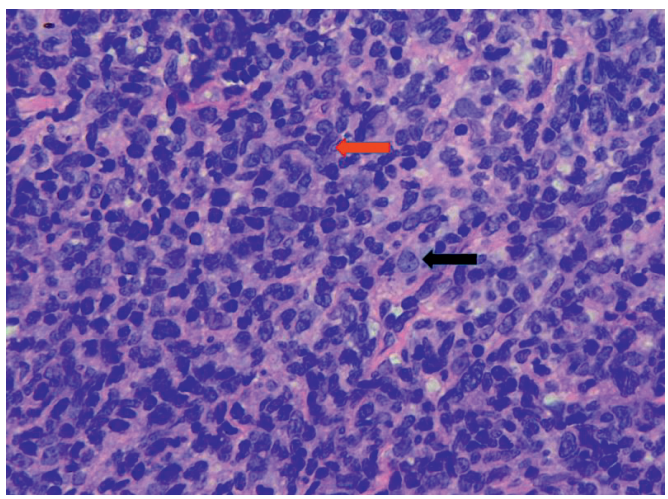

Figure 2C At high magnification, irregularly cleaved nucleus cells (centrocytes) are indicated by the red arrow, while prominent nucleoli with vesicular chromatin cells (centroblasts) are highlighted by the black arrow

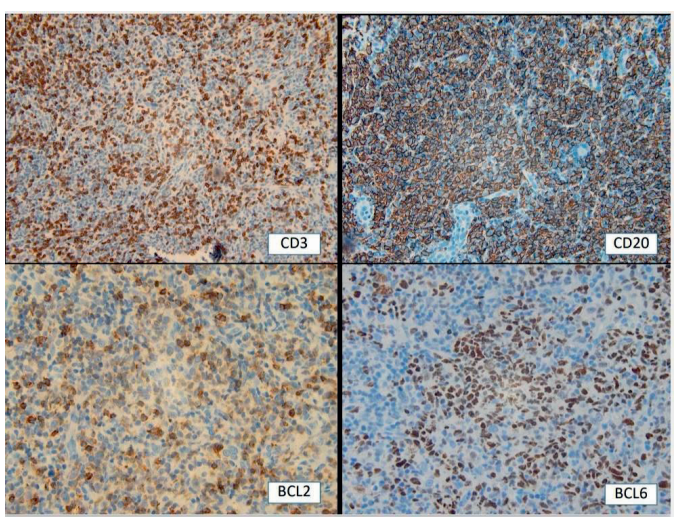

Figure 3 Immunohistochemical staining reveals positive results for CD20 and BCL6, while CD3 and BCL2 show negative results

Based on the clinical presentation, histopathological findings, and immunohistochemical stains, the diagnosis of primary cutaneous follicle center lymphoma (PCFCL) was established.

Discussion

Primary cutaneous follicle center lymphoma (PCFCL) represents the most prevalent form of cutaneous B-cell lymphoma, accounting for approximately 60% of cases within this category. It typically manifests in middle-aged individuals, with a notably higher prevalence among men.[1] The typical clinical presentation encompasses asymptomatic solitary or, less commonly, multiple erythematous or violaceous papules, plaques, nodules, or tumors of varying sizes, predominantly affecting the head, neck, or trunk, and infrequently the lower extremities.[2] Dissemination to other organs is rare, occurring in only 5-10% of cases.[3]

Histopathological analysis reveals three distinctive growth patterns: follicular, diffuse, and mixed. The prognostic significance of these patterns remains equivocal.[4] In the follicular pattern, lymphoid follicle formations in the dermis consist of centrocytes (cells with irregularly cleaved nuclei) and centroblasts (larger cells with vesicular chromatin and prominent nucleoli). Typically, the epidermis remains spared, with a visible grenz zone. Notably, the lack of tingible body macrophages and poorly defined mantle zones are characteristic features.[4] Conversely, the diffuse pattern entails dermal infiltration by tumor cells without follicle formation, while the mixed pattern encompasses a combination of follicular and diffuse patterns.[4]

Immunohistochemical staining demonstrates tumor cell expression of CD20, CD79a, and BCL6, with variable staining for BCL2, which is usually absent in most cases. The diffuse expression of BCL2 warrants consideration of secondary cutaneous involvement by systemic lymphoma. Differential diagnosis involves distinguishing PCFCL from reactive lymphoid hyperplasia, typically characterized by prominent tingible body macrophages and clearly defined mantle zones.

PCFCL generally carries a favorable prognosis, with a 5-year survival rate exceeding 95%.[4] Negative prognostic factors include lesions located on the legs, elevated lactate dehydrogenase (LDH) levels, the presence of more than two skin lesions, and the presence of nodular lesions.[2] Diagnostic evaluation includes a comprehensive medical history, physical examination, basic laboratory tests, LDH assessment, computed tomography, and flow cytometry. Staging adheres to the tumor-node-metastasis classification for cutaneous lymphomas other than mycosis fungoides/Sezary syndrome.[3]

The relationship between immunosuppressive agents and lymphoproliferative disorders has been documented. Long-term use of azathioprine in patients with inflammatory bowel disease has been associated with an increased risk of lymphoma.[5] Notably, all affected patients exhibited extracutaneous lymphoma involving both B and T cells[5], with azathioprine exposure durations ranging from 1 to 16 years. Risk factors for lymphoma development included advanced age, male gender, and prolonged duration of inflammatory bowel disease. The underlying mechanisms may involve the inflammatory processes inherent to inflammatory bowel disease itself, azathioprine exposure, or a combination thereof.[5]

Similarly, methotrexate (MTX), another immunosuppressive agent, has been linked to cutaneous lymphoproliferative diseases in the management of rheumatoid arthritis, dermatomyositis, Still's disease, and psoriatic arthritis. Treatment duration varied between 1 and 8 years among affected patients, all of whom experienced favorable outcomes following MTX discontinuation,

with resolution of the lymphoproliferative diseases.[6]

Systemic lupus erythematosus (SLE) confers an elevated risk of both systemic and cutaneous B-cell lymphoma[7], potentially attributable to dysregulated B-cell activation and defective apoptosis in autoimmune diseases.[8]

Our patient presented with PCFCL featuring a follicular growth pattern. Given her advanced age and hematologist's recommendation for supportive management, bone marrow examination was not pursued. Prolonged immunosuppressive therapy in the setting of underlying autoimmune disease likely contributed to the development of cutaneous lymphoma.

Treatment modalities for PCFCL encompass local radiotherapy and surgical excision, yielding nearly 100% complete remission rates[9], albeit with potential disfigurement and scarring.[10] Rituximab administration proves effective for multiple or extensive skin involvement, with multiagent chemotherapy rarely warranted.[9] Despite a relapse rate of approximately 30% following radiation or rituximab therapy, relapses typically remain confined to the skin.[9]

In our patient with multiple facial lesions, intravenous rituximab at a dosage of 500 mg/week resulted in complete lesion regression after four treatment cycles, without adverse events. A maintenance regimen of rituximab at a dosage of 500 mg every two months for two years is planned.

Conclusion

PCFCL can mimic tumid lupus erythematosus. Therefore, in cases of persistent or worsening tumid lupus erythematosus lesions, reevaluation with a skin biopsy is warranted.

Conflict of interest

The authors have no relevant conflicts of interest to disclose.

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Review Article

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Greater Mekong Subregion Medical Journal

Cancer-Associated Venous Thromboembolism

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Abstract:

Venous thromboembolism (VTE) presents a significant clinical challenge in the management of cancer patients, marked by a notably higher incidence compared to the general population. This article focuses on cancer-associated venous thromboembolism, exploring its multifaceted nature and the complexities encountered in both diagnosis and treatment. Additionally, the evolution of anticoagulant therapy, including the emergence of low molecular weight heparin (LMWH) and direct oral anticoagulants (DOACs), is examined for their efficacy in preventing recurrent cancer-associated VTE. Emphasizing the need for personalized treatment approaches. Through a comprehensive understanding of these challenges and advancements, clinicians can optimize therapeutic strategies to enhance outcomes for cancer patients at risk of VTE.

Keywords: Venous thromboembolism, Cancer, Management

Introduction

Blood clots in the veins, a condition known as venous thromboembolism, pose a growing challenge in modern medicine. While medications can dissolve these clots, they also carry a significant risk of causing bleeding incidence. VTE strikes cancer patients at a much higher rate than the general population, both at the time of diagnosis and upon later treatment duration. Treating VTE in cancer patients is particularly complex due to a confluence of factors. The cancerous condition itself, the direct complications it brings, and the side effects of treatments like surgery, radiation, and chemotherapy all contribute to VTE. Furthermore, even with anticoagulants for secondary prophylaxis, cancer patients have a sharp risk of recurrent blood clots and also higher potential for hemorrhage after treatment requires a different treatment approach for VTE in cancer patients compared to the general population.

Burden of venous thromboembolism in patients with cancer

Venous thromboembolism most commonly forms in the deep veins of the legs which this called deep vein thrombosis (DVT). These clots can then dislodge and travel to the lungs, blocking pulmonary arteries called pulmonary embolism (PE). Symptoms can range from leg swelling and

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pain to fever, shortness of breath, and even coma in severe cases. The general population experiences VTE at a rate of crudely 1 per 1,000 people.[1] However, this incidence elevates to 4-8 fold in cancer patients compared to those in the same age group.[2] Among the entire population of cancer patients, VTE occurs in up to 15%.[3] As high as 20% of newly diagnosed VTE cases involve patients with underlying cancer. In individuals diagnosed with VTE without a clear trigger (unprovoked venous thromboembolism), follow-up care reveals up to 10% of these patients develop cancer within 1-2 years.[4]

Pathogenesis and risk factors for VTE in cancer patients

The exact origins of VTE involve multiple theories. The most widely accepted explanation is Virchow's triad, proposed by Rudolf Virchow.[5] This triad identifies three key factors:

1. Stasis of blood: When blood flow slows in certain areas of the veins, such as around the valve cusps in the legs, or in cases of prolonged immobilization, the risk of clotting increases.

2. Endothelial injury: Damage to the endothelium allows platelets to come into contact with collagen, a protein in connective tissue. This contact triggers platelet activation and the clotting cascade, leading to clot formation.

3. Hypercoagulability: Certain genetic factors can predispose individuals to abnormal blood clotting. Conditions with Protein C, Protein S, and antithrombin deficiency fall into this category.

The current understanding suggests that multifactorial causes work together to cause VTE.[6] Cancer patients often have several of these risk factors, making them more susceptible to VTE compared to the general population. These risk factors can be categorized based on their origins as shown in table1.

Table 1 Risk factors of VTE in cancer patients

Patient-based factors	Cancer-based factors	Treatment-related factors
Age	Type of cancer	Chemotherapy
Underlying	Cancer stage	Radiation therapy
medical conditions	Metastatic	Surgery
Previous VTE	organ involvement	Hormone therapy
Genetic thrombophilia		Central venous catheter insertion
Obesity		

Symptoms, signs and diagnosis

The symptoms and signs of VTE in cancer patients are generally similar to those in the general population. The diagnostic tests used for VTE, such as D-dimer, ultrasound, CT scan, and venography, are also the same for both cancer patients and the general population. The choice of tests depend on the individual patient's clinical presentation and risk factors which are not mentioned here.

However, diagnosis of VTE in cancer patients can be challenging due to the

presence of other symptoms and signs related to the cancer itself or its complications. Such as edema from malnutrition, fever from infection, dyspnea from infection or anemia caused by chemotherapy and complications from cancer surgery. It is important to consider VTE in the differential diagnosis of any cancer patient with symptoms or signs that could be suggestive of VTE. A careful assessment is essential to avoid misdiagnosis.

Treatment of venous thromboembolism in cancer patients

The duration of anticoagulant therapy in cancer patients with thrombosis is not different from that of general patients. However, even with anticoagulant therapy, the recurrence rate of deep vein thrombosis (DVT) in cancer patients is still higher than in non-cancer patients.[7] In addition, after stopping anticoagulant therapy after completing treatment, cancer patients are twice as likely to have recurrent thrombosis as patients with DVT from other correctable causes.[8]

Anticoagulation Phase

1. Initial Phase (5 days-21 days) considered parenteral low molecular weight heparin (LMWH), unfractionated heparin (UFH) or direct oral anticoagulants (DOACs) such as rivaroxaban or apixaban.

2. Long-term Phase (5 days to 3-6 months) consider anticoagulation for all patients unless contraindicated.

3. Extended Phase (after 3-6 months) individualized decision-making depend on cancer status (active disease), treatment complications, bleeding risk, age and patient preference. Collaboration between healthcare providers and patients is essential. General recommendation is continuing anticoagulation if cancer is active or ongoing treatment is needed.

Evolution of anticoagulant options

The type of long-term anticoagulant therapy initially did not significantly differ from that recommended for non-cancer patients, where Vitamin K antagonists were the standard. Until 2003, Lee AY, et al.[9] reported findings from a randomized controlled trial comparing the efficacy of preventing recurrent VTE in cancer patients with DVT and PE who received either warfarin or dalteparin, a low-molecular-weight heparin (LMWH). It was found that the use of warfarin led to a higher incidence of recurrent VTE in cancer patients compared to dalteparin, with a hazard ratio (HR) of 0.48, though the probability of death did not significantly differ. A systematic review of 8 studies consistently showed that LMWH was more effective than warfarin in preventing recurrent VTE in cancer patients. Consequently, treatment recommendations largely advocate for the use of LMWH as the first-line therapy in managing cancer-associated thrombosis.[10]

However, LMWH has limitations for long-term use due to its subcutaneous administration, which may be inconvenient for medication management and could potentially exacerbate pain in cancer patients who commonly experience cancer-related pain. Currently, there are direct oral anticoagulants (DOACs) available, which have been studied for their efficacy in preventing recurrent venous thromboembolism (VTE) in cancer patients. Several randomized controlled trials, including the Hokusai VTE Cancer study[11], SELECT-D trial[12] and Caravaggio study[13] have compared the efficacy of DOACs (specifically edoxaban, rivaroxaban, and apixaban, respectively) versus dalteparin. The consistent finding across these studies is that DOACs are non-inferior to dalteparin in preventing recurrent VTE and can be used as anticoagulant therapy in cancer patients. However, patients

using edoxaban and rivaroxaban may have an increased risk of gastrointestinal bleeding in gastrointestinal cancer patients. Recently, a CANVAS study in 2023 compared the effectiveness of DOACs versus LMWH in preventing recurrent VTE in cancer patients. They found that DOACs were noninferior to LMWH in preventing recurrent VTE. Both groups had similar rates of major bleeding and adverse events.[14]

Although DOACs offer the convenience of oral administration and eliminate the need for monitoring coagulation levels, they still have limitations such as cost, accessibility, and interactions with other medications, predominantly through the cytochrome P450 enzyme system, particularly CYP3A4 and P-glycoprotein. These interactions include medications such as carbamazepine, phenytoin, protease inhibitors for HIV, azole antifungals, rifampicin, amiodarone, verapamil, diltiazem, and dronedarone.[15]

Current treatment recommendations for cancer patients with thrombosis suggest LMWH or DOACs over vitamin K antagonists.[16,17,18] Choice of anticoagulants take into account various factors including cancer type, disease status, bleeding risk, comorbidities, medication accessibility and convenience, financial status, and patient preference.

Table 2 Dosage and administration use of anticoagulant in VTE

ANTICOAGULANTS	DOSE
ENOXAPARIN	1 mg/kg SC every 12 hours (can consider decreasing to 1.5 mg/kg SC daily after first month)
TINZAPARIN	175 IU/kg SC once Daily
FONDAPARINUX	• 5 mg SC daily (< 50 kg) • 7.5 mg SC daily (50–100 kg) • 10 mg SC daily (> 100 kg)
BEMIPARIN	115 IU/kg SC once daily
UNFRACTIONATED HEPARIN (UFH)	80 units/kg IV bolus, followed by 18 units/kg/hour adjusted to target aPTT of 2–2.5 X control, followed by SC 250 units/kg every 12 hours
EDOXABAN	Initial therapy with heparin for at least 5 days followed by edoxaban 60 mg PO daily (or 30 mg PO daily in patients with estimated CrCl 30–50 mL/min or weight < 60 kg or concomitant potent p-glycoprotein inhibitors)
RIVAROXABAN	15 mg PO every 12 hours for the first 21 days followed by 20 mg daily
APIXABAN	10 mg PO every 12 hours for 7 days followed by 5 mg PO every 12 hours
DABIGATRAN	Initial therapy with heparin for at least 5 days followed by dabigatran 150 mg PO every 12 hours
WARFARIN	Initial with heparin, initial 2.5-5 mg PO daily adjusted to INR 2-3

Anticoagulant-related bleeding in CA-VTE; risk factors and management

Cancer patients with VTE face a difficult situation. While anticoagulant medications are essential to prevent new blood clots, they also increase the risk of bleeding. Recent large cohort studies have shown an approximation of a 10% bleeding event rate within a 12-month period of anticoagulant use. The most common clinically significant bleeding sites are the gastrointestinal tract, genitourinary tract, and intracranial hemorrhage, respectively.

Risk factors associated with anticoagulant-related bleeding in CA-VTE were: history of bleeding, estimated glomerular filtration rate (eGFR) < 60 ml/min, uncontrolled hypertension, predisposition to falling, history of ischemic stroke, alcohol abuse, anemia and liver disease had the highest association with anticoagulant-related bleeding. Of cancer specific variables, GI cancer, GU cancer and metastatic cancer was most predictive.[19]

The acute management of bleeding in cancer patients with VTE is generally similar to that in non-cancer patients. This may involve discontinuation of anticoagulant, specific antidotes, blood product replacement, using of bypassing agents and local control bleeding source, which is not mentioned in detail in this article.

The decision to restart anticoagulation therapy after a bleeding event depends on a careful evaluation of several factors; bleeding severity, risk of recurrent VTE is weighed against the risk of future bleeding. The likelihood of restarting anticoagulation therapy increases if the bleeding source has been effectively identified and addressed.

Patients should be informed about bleeding signs and symptoms and empowers patients to participate in a shared decision-making process with healthcare providers.

Recurrent VTE in cancer patients and consideration of extended therapy duration

The rate of recurrent VTE is higher in patients with persistent or unprovoked risk factors compared to those with transient risk factors. In cancer patients, several factors affect treatment continuity and VTE recurrence outcomes. These factors include: discontinuing anticoagulant medication early or not receiving the appropriate dosage, active cancer, particularly cancers of the pancreas, lung, ovary, or brain and needing to stop anticoagulation due to bleeding complications.

A 2018 COMMAND VTE registry study showed that the rate of discontinuing anticoagulation within a 1-year treatment period was highest in the cancer group compared to the transient risk factor and unprovoked groups (transient: 37.3%, unprovoked: 21.4%, cancer: 43.5% at 1 year, $P < 0.001$). Additionally, the cumulative 5-year incidences of recurrent VTE, major bleeding, and all-cause death were highest in the cancer group. The overall recurrent VTE rate in cancer patients was nearly 18% over the 5-year study period, which is 2.8 times higher than the transient risk factor group.[20]

In DOACs era, the COMMAND VTE Registry-2 study, conducted during 2015-2020, collected data from 5,197 patients. The study found that 79% of patients receiving oral anticoagulants were administered DOACs. Although cancer patients still had the highest bleeding event rate compared to the unprovoked or transient risk groups, the cumulative 5-year incidence of recurrent VTE in cancer patients was nearly 12%, which is a lower rate compared to the previous study.[21]

Due to the complexities of managing cancer patients, extended anticoagulation therapy should be considered for patients with active cancer who are undergoing ongoing cancer treatment without a high

risk of bleeding. Additionally, prolonged anticoagulation after cancer remission can be individualized for patients with an increased VTE risk and a low bleeding risk.

Conclusion

Cancer patients face a significantly higher risk (4-8 times greater) of developing blood clots (VTE) compared to the general population. This is due to the cancer itself, its complications, and side effects from treatments. Anticoagulants are crucial to prevent blood clots, but they also increase bleeding risk (around 10% within a year). Newer medications like LMWH and DOACs offer advantages over older options, but have limitations. Managing VTE in cancer patients requires careful consideration. Treatment decisions weigh factors like cancer type, bleeding risk, and ongoing treatment. Extended use of anticoagulants might be necessary for some patients with active cancer to manage their VTE risk. This underlines the importance of collaboration between healthcare providers and patients to create individualized treatment plans and achieve the best outcomes.

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