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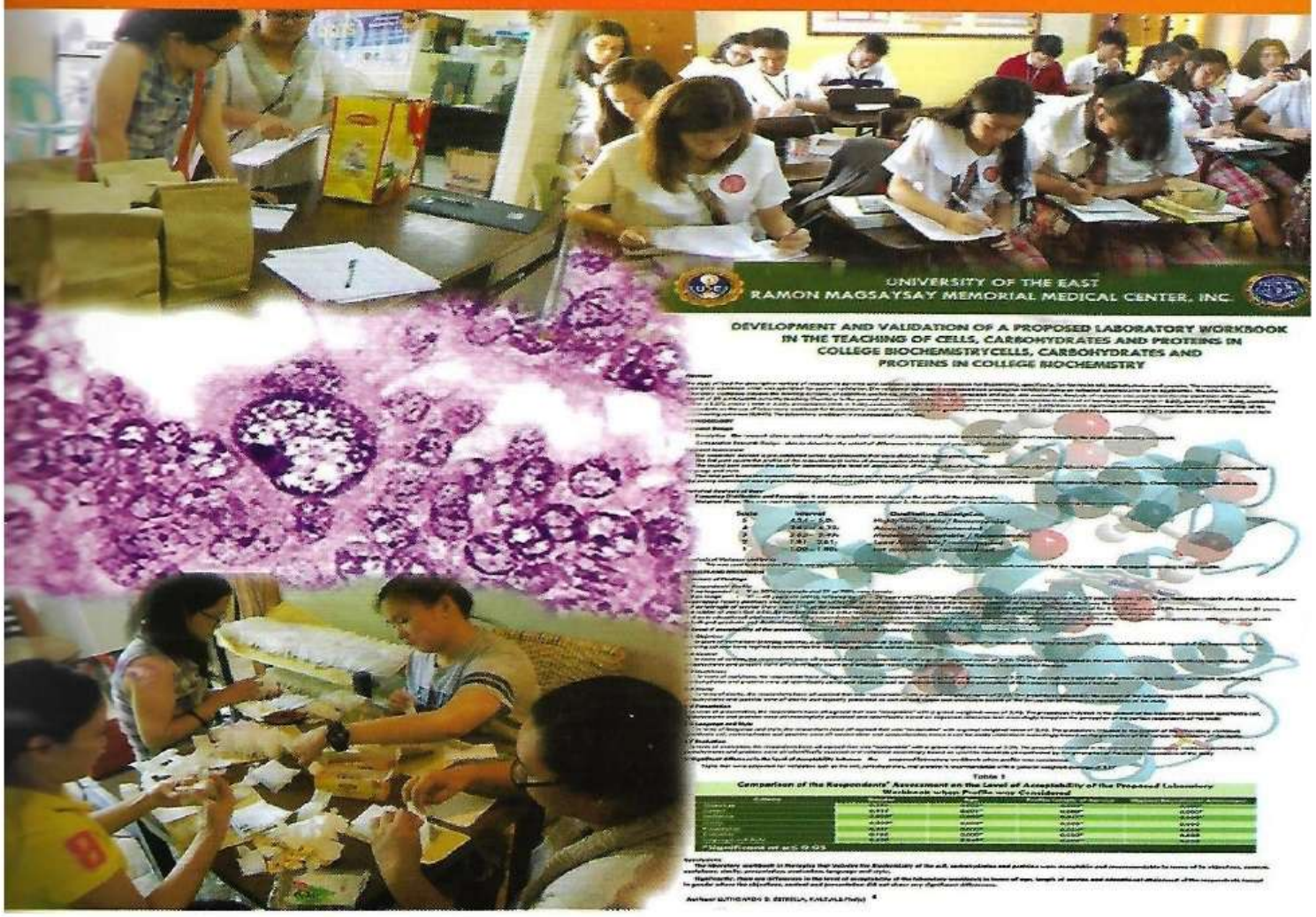

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A pilot randomized study comparing *Blumea balsamifera* (sambong) and terpenes on ureterolithiasis

Rommel P. Bataclan, MD and Tennille Tan, MD

Abstract

Introduction Alternative agents have been proposed for the management of kidney or ureteral stones. This study aimed to investigate the safety and efficacy of *Blumea balsamifera* (sambong) compared with a terpene combination drug as treatment for ureterolithiasis.

Methods Patients with clinically stable kidney function and ureteral stones of ≤ 5 mm were randomized to receive a special terpene combination (Rowatinex®) or *Blumea balsamifera*. All patients had a physical examination, and diagnosis of kidney stones was made by ultrasound at baseline and after 6 and 12 weeks of treatment. Primary outcomes were change in stone size and stone-free status, defined as obviously successful expulsion of calculi/fragments, documented by ultrasound.

Results After 6 weeks, five patients in the sambong group and six in the terpene group were stone free (p = 0.90). After 12 weeks, seven in the sambong and eight in the terpene group were stone free (p = 0.31). In terms of stone size, there was a significant decrease in the mean diameter in the sambong group (1.81 ± 2.01 mm, p = 0.008 and 1.12 ± 1.43 mm p < 0.005) and in the terpene group (1.24 ± 1.43 mm p<0.005 and 0.74 ± 0.70 mm, p<0.005) at 6 and 12 weeks, respectively. However, there was no significant difference between the two groups. Urine pH also increased in both groups compared to baseline but the difference was not statistically significant when comparing the two arms.

Conclusion *Blumea balsamifera* is comparable with a terpene combination in the dissolution of urolithiasis and is well-tolerated and safe.

Key words: Urinary calculi, terpenes, herbal medicine

The incidence of urinary tract stones in the Philippines is not available, however, among Asian countries, it ranges from 5 to 25%.[1] In a study done at a tertiary government hospital, this condition was found to be more common in males during the late adult period, usually presenting as bladder stones (cystolithiasis).[2] The possibility of recurrence increased with time, as approximately 10% would have had a new episode within a year, 50% in 5 to 10 years and up to 75% in 20 years.

There are different types of urinary tract stones. The most common type, even in the local setting, is calcium oxalate stones of the mixed type, which

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comprised almost 60% of the cases in the aforementioned local study.[2] Hypocitraturia is also another common problem, with lower urinary citrate found in Filipino stone formers, compared to non-stone formers.[3] Metabolic, radiologic and urinary investigations are therefore paramount in determining the type and severity of these stones.

Management may be either surgical or medical. Surgical treatment depends on the size, location, symptoms and presence of obstruction. If the ureteral stone is larger than 10 mm, and pain persists despite pain relievers, endoscopic removal may be done. However, if this is not possible, a ureteral stent or nephrostomy tube may be inserted until URS can be carried out. Extracorporeal shockwave lithotripsy, laser removal and percutaneous lithotomy are other options.[4]

Medical management meanwhile includes increased fluid intake and dietary modification.[4] Fluid intake should be primarily water and goal urine volume should be at least 2 liters daily. With regards to food intake, reduction in foods rich in oxalates, fats, animal protein have also been found to be beneficial. Dietary plans should be individualized, depending on the metabolic problems noted on work-up.

Pharmacologic treatment can also be given depending on the stone type. There are medications that also promote increased urine volume, stone expulsion and alkalinization of the urine. Terpenes is one of these medications that have been investigated in various studies. Its exact mechanism of action is not known but some of these terpenes include pinene and fenchone, which are said to have anti-bacterial properties. Cineole and anethole meanwhile exert anti-inflammatory and analgesic activities. Camphene and borneol were shown to have anti-spasmodic effects on smooth muscles in animal studies.[5]

In a randomized placebo-controlled trial by Engelstein in 1992, terpenes had a significantly higher expulsion rate of ureterolithiasis (81% vs. 59%) with a good safety profile.[6] However, in another study in patients with distal ureteral stones less than 10 mm in diameter, terpenes showed lower expulsion rates than tamsulosin.[7] It also had varying stone clearance rates among post-extracorporeal shock wave lithotripsy patients in placebo-controlled trials.[8,9]

In the Philippines, *Blumea balsamifera* (known locally as sambong) has also been used as part of medical management of urinary tract stones. Sambong is a coarse, erect, strongly aromatic shrub commonly found in open grasslands. It has been used as herbal medicine for fever, headache, boils, abdominal pain, cough and gaseous distention. It was discovered accidentally as a diuretic when initial studies for other medicinal purposes noted that subjects complained of increased frequency of urination.[10] A pilot study by de Leon and Maramba in 1984 showed that sambong had comparable diuretic properties with thiazide, had a rapid onset (within 30 minutes), and did not have any significant effect on serum electrolytes.[11]

In the 1990s, there were further studies on sambong as part of urinary tract stone treatment. In a randomized, double-blind placebo-controlled trial by Sigua and Molina, there was a higher proportion of patients with complete passage after 4 weeks of sambong compared to placebo (31% vs. 8%) and significant reduction of stone size based on radiographic imaging.[12] Another trial showed a higher rate of complete passage (55%) compared to placebo.[13] Almost 90% of the patients had radiographic improvement of the stone and there were similar rates of acceptability in terms of taste, smell and ease of swallowing.

The only head-to-head study comparing sambong with another medication was an open label study with potassium citrate.[14] No other published studies have been done on sambong for urinary tract stones. This pilot study investigated the comparability of sambong with terpenes in terms of dissolution effect and safety among patients with non-obstructing urolithiasis.

Methods

The study was done from January to June 2017 at the San Antonio District Hospital, a 50-bed primary level facility ran by the Provincial Government of Nueva Ecija. The study was approved by the Provincial Health Office and the hospital's Ethics Committee. The subjects comprised of clinic patients newly diagnosed with ureterolithiasis. Initial screening through history taking and physical examination was done. Patients included were adults 18 years old and above with ureterolithiasis up to 5

mm based on ultrasound. Subjects were excluded if they had 1) clinical signs of urinary tract obstruction, 2) active infection, 3) renal insufficiency defined as estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73m^2 by MDRD equation, and 4) patients on diuretics regardless of the indication.

Informed consent was obtained from each patient. Afterwards, baseline laboratory work-up with urinalysis and blood chemistries were obtained. A baseline ultrasound was performed. The operator and reader were blinded to the clinical data of the subjects, other than the diagnosis of urinary tract stones. A research assistant randomized the patients to either Group A where patients received sambong 500mg/tablet, taken two tablets, three times a day or Group B, who were given the terpene combination (Rowatinex®) two capsules, three times a day for three months. Both medications were packaged in blister packs and placed in opaque envelopes marked A or B. In addition, all patients were given tamsulosin 400ug/tablet, one tablet daily. Instructions on proper diet and increased fluid intake were given.

Patients were instructed to follow-up weekly on the first month to monitor for adverse events or other medical concerns. On the 6th week, patients were requested to follow-up for repeat diagnostics and ultrasound. If there were no problems, follow-up was done every two weeks until the end of the third month (12 weeks). Another set of blood chemistries, urine testing and ultrasound were performed. A subject who failed to come back at least twice was classified as drop-out and the reason for dropping out was recorded.

The primary outcome of the study was complete dissolution of stone, as documented on ultrasound. Other outcomes include stone size, urine pH, serum chemistries and adverse outcomes. Other than the adverse events, the variables were collected at 6 and 12 weeks of treatment. Non-numerical variables were expressed as frequencies with percentages and analyzed by chi-square test. Numerical variables were expressed as mean + standard deviation (SD), and analysis of variance (ANOVA) was done.

Results

Forty subjects were recruited in the study from January to June 2017, 20 in each arm. Before the 4th week, three subjects from each group were dropped for lack of compliance, leaving 17 in each treatment arm. Table 1 shows the baseline characteristics of both treatment groups. There were no statistical differences among the variables presented. All lithiases were in the mid- to distal third of the ureter.

Table 1. Baseline characteristics of 34 subjects.

	Sambong Group (n=17) n (%)	Terpene Group (n=17) n (%)
Gender		
Male	8 (47.1)	7 (41.2)
Female	9 (52.9)	10 (58.8)
Age (years ± SD)	47.6 ± 14	47.5 ± 12
Co-morbidities		
Diabetes	2 (11.8)	4 (23.5)
Hypertension	3 (17.6)	4 (23.5)
Dyslipidemia	6 (35.3)	5 (29.4)
Laterality		
Left	6 (35.3)	8 (47.1)
Right	11 (64.7)	9 (52.9)
Other tract stones		
Nephrolithiasis	2 (11.8)	4 (23.5)
Cystolithiasis	1 (5.9)	0

Table 2 shows the primary stone outcomes of both treatment groups. After 6 weeks, five patients in the sambong group and six subjects in the terpene group were stone-free ($p = 0.90$). After 12 weeks, 41.2% in the sambong group and 47.1% in the terpene group were stone-free ($p = 0.31$). In terms of stone size, there was a significant decrease in the mean stone size after 6 weeks (1.81 ± 2.01 mm, $p = 0.008$) and 12 weeks (1.12 ± 1.43 mm $p < 0.005$) in the sambong group, and in the terpene group (1.24 ± 1.43 mm, $p<0.005$ at 6 weeks and 0.74 ± 0.70 mm, $p < 0.005$ at 12 weeks). However, there was no significant difference between the two groups. Urine pH also significantly increased in both groups compared to baseline but the difference between the two arms was not significant.

Table 3 shows the serum chemistries in both groups. There were no significant differences in the serum sodium, potassium, creatinine and ionized calcium between the treatment arms. However, serum

uric acid in the sambong group showed a significant decrease after 12 weeks of treatment compared to the terpene group. There was also a significant decrease in the serum uric acid in the sambong group compared at their baseline values and at 6 weeks of treatment.

Table 2. Stone outcomes on patients treated with sambong and terpenes.

	Stone Size (mm)		Stone Free		Stone Unchanged		Stone Decrease Size		Urine pH	
	Sambong	Terpene	Sambong	Terpene	Sambong	Terpene	Sambong	Terpene	Sambong	Terpene
Baseline	2.98±1.02	3.01±0.88							5.82±0.34	5.85±0.55
6 weeks (p vs baseline)	1.81±2.01 (0.008)	1.24±1.43 (<0.005)	5	6	3	1	9	11	6.64±0.30 (<0.005)	6.41±0.35 (0.02)
P-value in 2 groups	0.22				0.9				0.23	
12 weeks (p vs baseline)	1.12±1.43 (<0.005)	0.74±0.70 (<0.005)	7	8	3	3	8	6	6.64±0.14 (<0.005)	6.58±0.19 (<0.005)
P-value in 2 groups	0.30				0.31				0.68	

Table 3. Serum chemistries of sambong and terpene groups

	Sambong Group (n=17)	Terpene Group (n=17)
Serum Na (mmol/L)		
Baseline	142.2 ± 21	142.2 ± 77
6 weeks	141.6 ± 12	142.3 ± 11
12 weeks	142.1 ± 13	141.5 ± 14
Serum K (mmol/L)		
Baseline	4.2 ± 0.15	4.3 ± 0.18
6 weeks	4.2 ± 0.10	4.3 ± 0.07
12 weeks	4.2 ± 0.09	4.2 ± 0.04
Ionized calcium (mg/dL)		
Baseline	4.9 ± 0.03	5.0 ± 0.04
6 weeks	4.9 ± 0.04	5.1 ± 0.02
12 weeks	5.0 ± 0.03	5.0 ± 0.02
Serum creatinine (mg/dL)		
Baseline	1.1 ± 0.05	1.0 ± 0.05
6 weeks	1.1 ± 0.04	1.0 ± 0.02
12 weeks	1.1 ± 0.06	1.1 ± 0.08
Serum uric acid (mg/dL)		
Baseline	6.3 ± 0.77	6.3 ± 0.47
6 weeks	6.2 ± 0.45	6.2 ± 0.32
12 weeks	6.0 ± 0.16[a,b,c]	6.1 ± 0.17

Note: [a] p = 0.02 vs uric acid terpene at 12 weeks
[b] p = 0.01 vs uric acid sambong at 6 weeks
[c] p = 0.003 vs uric acid sambong at baseline

There were no differences in adverse events and only mild symptoms were reported. There were 3 and 5 episodes of nausea in the sambong and terpene groups, respectively. Four subjects in sambong group and three in the terpene group developed urinary tract infections. All UTIs showed mild pyuria and were treated accordingly with antibiotics. No hospitalizations nor deaths were noted.

Discussion

In non-obstructing urinary tract stones, medical management is a practical and acceptable treatment. The terpene drug used in this study is a combination of seven essential oils with the previously mentioned effects. It may promote diuresis through increased renal blood flow. It was introduced in the 1950s and still used worldwide as part of medical management. In the present study, the stone-free rates of patients given terpenes are comparable with previous studies by Engelstein in 1992 and Aldemir.[6,7] Most of the studies published on efficacy are case reports and majority had a duration of only 4 weeks.

Sambong, meanwhile has been used locally and in other tropical countries but available data on efficacy are limited. The only published randomized trial compared sambong with placebo and potassium citrate.[14] Results showed sambong had a 37% stone-free rate at the end of 2 months, compared to 25% in the placebo and 50% in the potassium citrate groups; the present study had a rate of 41%. Compared with placebo, sambong also showed significant decrease in mean stone size, which was also the trend in the present study.

The study shows that patients treated with sambong had statistically similar stone dissolution rates. However, in terms of average stone size, those treated with sambong had a smaller mean diameter than those given terpenes. Multiple mechanisms have been elucidated. In a kinetic study, sambong increased crystallization and nucleation rates, leading to tendency to form smaller-sized crystals which are easier to eliminate.[15] As a diuretic, it significantly increased urine volume, and urine sodium and chloride excretion with minimal kaliuresis.[11] As mentioned earlier, its diuretic effect was comparable to thiazides, which is given in cases with hypercalciuria. It is also said to have muscle relaxant properties.[16]

Another result in this study was a significantly lower serum uric acid among patients treated with sambong. Its uric acid lowering ability may be due to xanthine oxidase inhibition. In a study comparing different medicinal plants available locally, *Blumea balsamifera* was shown to have the highest xanthine oxidase inhibition at 79.67%, with *M. pudica* having the next highest inhibition at 62.36%.[17] It should be noted that allopurinol was given to five patients in the sambong group and four in the terpene group. However, there was no significant difference with the proportion of those given uric acid lowering medications, hence the interventional drug may have contributed to the lowering of mean serum uric acid. The study also showed a good safety profile in those treated with sambong and terpenes. This increases compliance of the medication, possibly making it more efficacious.

This is the first study on ureterolithiasis that compared sambong with terpenes. The strength of this study was that the treatment duration was longer (12 weeks) as compared to other randomized trials. It focused on a specific type of urinary tract stone (ureterolithiasis) to avoid heterogeneity. Also, most studies of this nature focused only on stone-free rates. This study included some serum chemistries, which are recommended by guidelines to be a part of work-up to determine possible stone type and the need for adjunct medications.[18]

The study has several limitations. While treatment covered 12 weeks, it was not long enough to determine long-term effects and recurrence rates. The only urinary test done was a routine urinalysis. Ideally, other urine chemistries should also be performed to determine other possible causes of stone formation. Despite these limitations, the study showed that treatment with *Blumea balsamifera* in patients with small-sized ureterolithiasis is comparable to terpenes in terms of efficacy and is well-tolerated and safe.

Conflict of interests None to declare

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A randomized controlled clinical trial on the effectiveness of cinnamon tea in reducing menopausal symptoms among perimenopausal women

Marie Antonette O. Feliciano, Franchesca N. Felix, Beatrix Maria Lilia A. Fider, Frances D. Fontanilla, Anna Katerina R. Francisco, Diorella Mae S. Gatapia, Mariah Carla V. Gonzales, Paul Nichol G. Gonzales, Yoni Benjamin G. Gonzales, Chloe Stephanie O. Gotianse, Jose Ronilo G. Juangco, MD, MPH (Faculty Adviser)

Abstract

Introduction Women in the perimenopausal period experience the height of menopausal symptoms due to the fluctuating levels of hormones because of ovarian dysfunction. This study aimed to determine the effect of cinnamon tea on menopausal symptoms among perimenopausal women.

Methods Perimenopausal women from Cainta, Rizal were recruited using cluster sampling and were randomly allocated into cinnamon tea or black tea groups. All participants were instructed to consume one tea bag once a day for 28 days. A response survey was conducted by the researchers using the Menopausal Rating Scale questionnaire every 2 weeks during the 28-day period to assess the number and severity of symptoms associated with perimenopausal stage.

Results The Menopausal Rating Scale scores of both cinnamon and placebo groups showed a statistically significant decrease in the number and severity of symptoms over time within groups. However, there was greater decrease in symptom number and severity among the cinnamon tea group and the difference was significant.

Conclusion Cinnamon tea resulted in a decrease in the severity of perimenopausal symptoms and may be an effective, economical and accessible alternative treatment for perimenopausal symptoms.

Key words: Cinnamon, perimenopausal symptoms

Menopause is a significant concern of most women due to the burdensome physical and psychosocial symptoms they experience. It occurs usually in a constant age, regardless of the race, age at menarche, socio-economic status or number of previous ovulations. However, menopausal symptoms may be experienced years prior the cessation of menstruation; this is also known as the perimenopausal stage. This is caused by fluctuating hormones, marking a shift from normal ovulatory cycles to the end of menstruation.[1,2] Estrogen deficiency associated with decreasing follicular function is the main factor for the major effects of menopause, affecting women both physically and psychologically.[3] During the perimenopausal

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transition, menstrual irregularity increases and many women experience symptoms of menopause, prompting them to seek health care.[4,5]

One of the standard treatments to alleviate the symptoms of menopause is menopausal hormonal therapy (MHT).[5] This includes estrogen, progesterone, or estrogen-progesterone therapy.[6] MHT regulates the intact hypothalamic-pituitary axis during the perimenopausal period, thus alleviating a woman's symptoms of menopause. However, there are undesirable effects related to MHT use, prompting women to seek alternative treatments in the form of "natural therapies" in relieving menopausal symptoms. These include minerals, vitamins, soy herbs, isoflavones, and custom compounded hormones.[7] Cinnamon may be one of these natural remedies for menopausal symptoms.

Cinnamon is a member of the laurel plant family; the dried inner bark of its tree has been used as a spice for thousands of years. Besides being used as a flavoring and scent for cosmetics, food, and liquor, cinnamon's properties are used for health benefits as well. Cinnamon tea has been demonstrated to selectively stimulate the production of progesterone in human adrenocortical cells through its component, cinnamaldehyde. Cinnamaldehyde comprises most of the oils of cinnamon (65-90%) with the other essential oils making up the remaining 1-8%. A different study found levels between 13.1 and 56.9mg of cinnamaldehyde per gram of cinnamon.[8] Another study showed that a dose-dependent increase in progesterone in a culture medium resulted from the exposure to cinnamaldehyde.[9] The consumption of cinnamon which contains cinnamaldehyde can help increase levels of progesterone. Pharmacological studies have been done on cinnamon's effects in treating gynecological problems related to irregular menstruation and menopause.[10] In addition, cinnamon is readily available and affordable. This study aimed to determine the effectiveness of cinnamon tea in reducing the menopausal symptoms of identified perimenopausal women.

Methods

A randomized single-blind, placebo-controlled clinical trial was conducted to determine if cinnamon could effectively reduce the severity of perimenopausal symptoms. Women from Barangay San Juan, Cainta, Rizal were recruited and allocated to receive either cinnamon or black tea for one month. The severity of symptoms was measured using a Filipino translation of the Menopausal Rating Scale. The research was approved for implementation by the UERMMMCI Research Institute for Health Sciences Ethics Review Committee.

Healthy perimenopausal Filipino women 39 to 51 years old residing in Barangay San Juan, Cainta, Rizal were selected using cluster random sampling of female residents from the sampling population. A random online generator was used to select one from among 40 sitios in the town. Excluded subjects were those currently on hormonal therapy and those taking medications including oral contraceptives and herbal medicines for menopause. The sample size for each comparison group was calculated using the SD_1 (2.91) and SD_2 (4.33), μ_1 (2.73) and μ_2 (0.026) that were taken from the study on Aphrodit capsule as management for menopausal symptoms. The sample size computed is eight for each group with a confidence interval of 99% and power of 90%.[11]

Subjects included in the study were interviewed to obtain demographic data and menopausal symptoms using the Filipino translation of the Menopausal Rating Scale (MRS) questionnaire, the results of which served as the study's baseline data (MRS 1). Subjects were then randomly allocated into treatment and control groups. The treatment group was given 1g of cinnamon in their tea per day, while the control group were assigned to 1g of placebo per day. Both groups underwent the trial for one month. The placebo used for this study was black tea, made from the leaves of the *Camellia sinensis* plant. The survey was conducted three times: at the start of the trial (MRS 1), after two weeks (MRS 2), and at the end of the month (MRS 3).

The MRS is a scale used to score symptom severity, which is defined by the frequency of occurrence of each menopausal symptom. The MRS questionnaire was translated from English to Filipino and then from Filipino to English by two different Filipino professors. The scale is comprised of 11 core symptoms divided into their three dimensions (subscales) - psychological (depressed, irritable, anxious, exhausted), somato-vegetative (sweating/ flushing, cardiac complaints, sleeping disorders, joint & muscle complaints), and urogenital (sexual problems, urinary complaints, vaginal dryness). The severity of symptoms was measured using a 5-point Likert scale, with each increasing point representing

increasing severity (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe). The sum of the scores for each subscale was added and made up the total score, the highest of which is 44.[12] A higher MRS score meant more severe symptoms.

The internal consistency of the MRS scale measured with Cronbach's alpha showed coefficients that varied between 0.6 and 0.9 across countries for the total score and the three sub-scales. The test-retest correlation coefficients (Pearson's correlation) of the total score was 0.9 for all countries, indicating good measure of internal consistency. In a large multinational survey in nine countries, similar factor loadings of the 11 items from the three domains of the MRS scale were observed. This suggests that the MRS scale measures the same phenomenon in different countries and that it can be used as well in clinical studies.[12]

Identical looking marked bags of either cinnamon tea or placebo (black tea), which were unknown to both the researcher and the respondents, were placed in a non-transparent container. The researcher indiscriminately took one bag from the container and gave it to the respondent. After handing out the bag, the researcher checked and identified the mark on the bags that differentiated cinnamon tea from black tea. Group assignment was then noted by the researchers on the first visit. Participants in the experimental group were given cinnamon tea (1g of cinnamon powder served in hot water, once a day), while the control group was given a placebo (1g black tea served in hot water, once a day). Participants took the tea once a day for four weeks.

For the duration of the clinical trial, the participants were contacted via phone call once a week and an SMS was sent to each participant every day to remind them to take the assigned tea. Random visits were also conducted wherein the used and remaining tea bags were checked to ensure the compliance of the participants.

Identification of variables that might influence the findings was analyzed by testing the differences between groups using Chi-square. The significance of the difference in MRS scores across time and between groups was determined using mixed MANOVA and MANOVA, respectively. The analysis of this study was performed using the IBM Statistical Package for the Social Sciences (SPSS).

Results

Forty-two perimenopausal women were included in the study, with 22 assigned to the cinnamon tea group and 20 to the black tea group. Their mean age (45.9 vs 45 years) and age at menarche (12.8 vs 13.3 years) were comparable. Around 90% of the women had their menarche at 15 years or younger. The distribution of the subjects in terms of the other demographic parameters between the cinnamon tea and black tea groups was comparable, as seen in Table 1. There was no significant difference between the baseline MRS scores of the cinnamon tea and black tea groups.

As shown in Table 2, the cinnamon tea group's baseline scores were lower than the placebo group's (MRS 1) though the difference was not significant ($p = 0.405$). For MRS 2, cinnamon tea group's scores

Table 1. Comparison of the clinic-sociodemographic characteristics of 42 subjects.

Characteristics	Cinnamon tea n (%)	Black tea n (%)	p-value
Frequency	22 (52.4)	20 (47.6)	0.76
Age (yr)			0.38
39-44	7 (16.7)	9 (21.4)	
45-51	15 (35.7)	11 (26.2)	
Age of menarche (yr)			0.25
10-15	21 (50.0)	17 (40.5)	
16-20	1 (2.4)	3 (7.1)	
Religion			0.26
Catholic	18 (42.9)	18 (42.9)	
Christian	4 (9.5)	1 (2.4)	
Muslim	0 (0)	1 (2.4)	
Civil Status			0.23
Single	6 (14.3)	6 (14.3)	
Married	13 (31.0)	14 (33.3)	
Widowed	3 (7.1)	0 (0)	
Education			0.60
Elementary	3 (7.1)	5 (11.9)	
High school	16 (38.1)	14 (33.3)	
College	2 (4.8)	1 (2.4)	
Vocational	1 (2.4)	0 (0)	
Occupation			0.67
None	1 (2.4)	2 (4.8)	
Housewife	9 (21.4)	6 (14.3)	
Skilled worker	5 (11.9)	3 (7.1)	
Government	3 (7.1)	2 (4.8)	
Commerce	4 (9.5)	7 (16.7)	

were lower than placebo's. For MRS 3, cinnamon tea group's scores were lower than placebo's. Table 2 shows a decrease in the MRS scores from baseline to week 4 with the cinnamon tea group showing a larger decrease. Mixed MANOVA shows that the decrease across time is significant ($p < 0.05$). MANOVA shows that the difference in the decrease between the cinnamon tea and black tea groups is significant ($p < 0.05$).

Table 2. Comparison of Menopause Rating Scale (MRS) scores.

	Cinnamon tea	Black tea	p-value
MRS 1	10.09	12.05	0.405
MRS 2	3.82	9.20	0.009
MRS 3	2.86	6.20	0.109
Mixed MANOVA	F (1.41, 53.49) = 34.95		< 0.05
MANOVA	F (1, 38) = 5.35		< 0.05

None of the participants experienced any allergic reaction or adverse events while taking either cinnamon or black tea.

Discussion

In this study, the effectiveness of cinnamon tea in comparison with placebo in perimenopausal women was evaluated. The MRS scores of the cinnamon tea group and the placebo tea group showed a statistically significant decrease in number and severity of symptoms throughout the study. However, there was greater decrease in symptom in the cinnamon tea group.

It is shown that there is a decrease in severity of symptoms in MRS measures within subjects across time. The researchers observed the reduction of symptoms from baseline, up to four weeks after taking the treatment. The results showed that symptoms significantly decreased across time. The symptoms were highest during the baseline measurement, then decreased two weeks after consuming the teas, and were lowest after four weeks. The decreases between the different points are all independently significant. This indicates a general reduction in symptom severity of the participants, weeks after consuming the tea. The MANOVA showed that the consumption of tea significantly reduced the severity of symptoms, however, the type of tea is significant. Particularly, the cinnamon tea group experienced significantly less symptoms than the placebo group.

The results of the study showed that cinnamon tea significantly reduces perimenopausal symptoms. This is consistent with a study on the effect of Aphrodit capsule, consisting of 40 mg of *Tribulus terrestris* fruits, 12.27 mg ginger, 33 mg saffron and 11 mg of cinnamon, on somatic symptoms of postmenopausal women. The study also used the Menopausal Rating Scale as their tool with a four-week duration. They concluded that Aphrodit capsule reduces hot flashes, sleep and musculoskeletal disorders in postmenopausal women.[11] Another study showed a significant decrease in menopausal hot flashes with the use of Gui Zhi Tang, a cinnamon twig decoction with added flavors.[13]

In conclusion, this study shows that the consumption of cinnamon tea demonstrated a decrease in the severity of perimenopausal symptoms and may be an effective, economical and accessible alternative treatment for the reduction of the severity of perimenopausal symptoms.

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Awareness of physical therapy among Grade 10 students under the K-12 Program

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Abstract

Introduction This study determined the level of awareness of Grade 10 junior high school students on physical therapy education, scope of practice, their source of information, and aimed to identify factors resulting in non-familiarity of the students on physical therapy.

Methods Grade 10 junior high school students were recruited from three private schools in the National Capital Region through non-probability sampling techniques. The students completed a self-administered survey questionnaire. Descriptive statistics focused on frequency distribution.

Results Most of the 387 respondents were aware of the discipline (physical therapy), with 31% of them answering that their family was their primary source of information. Many thought Bachelor of Science in Physical Therapy was a four-year course, with human anatomy being one of the major subjects. The respondents also knew that a licensure examination was essential to practice physical therapy. They also expected physical therapists to offer different treatment modalities, such as exercises, massage therapy, hot and cold packs for various musculoskeletal disorders. Respondents also viewed the work of physical therapists to be hospital-based, with average monthly income ranging from PhP 12,000.00 to PhP 20,000.00. On the other hand, students who were unaware of physical therapy did not have relatives who were health professionals and appeared to be uninterested in pursuing any health or science-related degree program in college.

Conclusion Even though most of the students were aware of physical therapy as a profession, majority of them lacked knowledge as to physical therapy education and scope of practice.

Key words: Physical therapy education, awareness, Grade 10 junior high school students

Physical therapists play essential roles in today's healthcare system and are recognized as vital providers of rehabilitation and habilitation, and prevention and risk-reduction services.[1] Since its introduction in the Philippines in the early 1960s, physical therapy has progressively evolved as a specialty discipline, expanding its scope of functions, treatments, and settings, while the responsibilities of licensed physical therapists have been appropriately modified to adapt to changes in the holistic management of patients.[2] Despite the pivotal function of physical therapists in the healthcare system, they

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are still erroneously viewed as mere masseurs by the general population, and are often unrecognized as legitimate healthcare professionals. Adding to the dilemma is the paucity of published literature on the public's perception on the clinical value of physical therapy and rehabilitation medicine.[3]

The Philippines has a new educational system called the K to 12 (K-12) Program, duly recognized and implemented in 2016 by the Department of Education. The K-12 Program requires kindergarten and 12 years of basic education, covering six years of elementary school, four years of junior high school, and two years of senior high school (SHS). Senior high school students are given the prerogative to pursue any academic track of their interest, i.e., General Academic Strand (GAS); Humanities and Social Sciences (HUMS); Science, Technology, Engineering, and Mathematics (STEM); and Arts and Designs (AD). This revised curriculum aims to provide SHS students adequate time and preparation for their chosen field, by giving more opportunities to master basic concepts and develop pertinent skills that will prepare them for either tertiary education or middle-level skills enhancement, employment, and entrepreneurship, as they continue to be life-long learners in their preferred career paths.[4] The new K-12 curriculum is viewed to be beneficial for the Filipino students, especially for those who will seek employment immediately after their SHS graduation.

Given the new K-12 curriculum program, will this impact on the practice of physical therapy in the Philippines? How do students now perceive physical therapy as a potential future career path, and how attractive is the Bachelor of Science in Physical Therapy degree program to the SHS graduate? Are there gaps in the K-12 program that need to be addressed to prepare the SHS students, especially those in the STEM track, for pursuing physical therapy as a degree program in college? This study aimed to determine the level of awareness of grade 10 junior high school students on physical therapy as a collegiate course and potential future career undertaking.

Methods

This was a descriptive cross-sectional survey conducted in three selected private high schools in the National Capital Region. Grade 10 junior high school students were recruited using non-probability convenience sampling. In coordination with the school administration officials, informed consent/ assent were obtained from the prospective respondents during regular class hours within school premises. Participation in the study was purely voluntary, and the data gathering procedure was executed following an exam-type of protocol in answering the questionnaire. Data were collected using a self-administered questionnaire. The survey tool asked about awareness of physical therapy, sources of information, aspects on physical therapy education and practice, what a physical therapist does and uses, where they work and plans after graduation from senior high school. Descriptive statistics were performed to determine frequencies and proportions.

The researchers utilized a self-administered questionnaire, patterned from a previous similar study. The tool was pilot-tested and underwent face validation. In addition, some faculty members from the UERMMMCI College of Allied Rehabilitation Sciences performed content validation. After several revisions, the questionnaire was finalized and used in this study. The study was approved the Ethics Review Committee of the UERMMMCI Research Institute for Health Sciences.

Results

Out of 378 Grade 10 junior high school students from three private schools, majority were males, 16 to 17 years old, and coming from urban centers, as seen in Table 1. Seven out of 10 students knew of physical therapy and 90% got their information from parents, media, friends and teachers (Table 1). Media sources included television and radio commercials, print ads and news articles, online sources, and social media networks.

As seen in Table 2, more than half of respondents thought that BS Physical Therapy was a 4-year course and had fair knowledge of what physical therapy students studied. Almost 70% correctly answered that physical therapists need to pass the licensure examination given by the Professional Regulations Commission to practice. Three-fourths of those surveyed thought there was average difficulty in finding work within a year of graduation; perceptions regarding income earned if they practiced

in the country were almost evenly distributed from a low to moderate range.

More than half of the respondents said that physical therapists treat patients with exercise, massage and other modalities and that they treat sports injuries. More than 10% thought that physical therapists give massages in spas or as home service. Respondents thought that physical therapists treated patients with muscle pains, sprains, fractures or stroke using heat or cold, x-rays, bandages or used parallel bars, as seen in Table 3. Majority thought that physical therapists worked in hospitals, sports clinics and public health departments (Table 4).

Table 1. Characteristics of 378 Grade 10 respondents from three private schools.

Variable	Number (%)
Age (yr)	
15	68 (18.0)
16	174 (46.0)
17	81 (21.4)
18	42 (11.1)
> 18	13 (3.4)
Sex	
Male	207 (54.8)
Female	171 (45.2)
Place respondent grew up	
City/urban	337 (89.2)
Province/rural	41 (10.8)
Heard of physical therapy	
Yes	265 (70.1)
No	113 (29.9)
Source of ideas about physical therapy	
Family	83 (31.3)
Media	60 (22.6)
Friends	52 (19.6)
Teachers	40 (15.1)
School advertisements	23 (8.7)
Others	7 (2.6)

More than 90% said they wanted to pursue a college course after senior high school but only 3% were interested in a health-related course (Table 5).

Discussion

Age had been identified as an important factor in determining level of knowledge and awareness of

Table 2. Perception of 265 respondents about physical therapy education and practice.

Variable	Number (%)
Course duration (yr)	
≤ 1	22 (8.3)
2	28 (10.6)
4	146 (55.1)
5	60 (22.6)
> 5	9 (3.4)
Subject area	
Human body	158 (32.6)
Exercises	132 (27.2)
Sports injuries	119 (24.5)
Diseases	38 (7.8)
Others	38 (7.8)
Qualification to practice	
After graduation	53 (20.0)
Passing PRC examination	183 (69.1)
Passing civil service examination	18 (6.8)
Others	11 (4.1)
Difficulty in getting employed	
Easy	28 (10.6)
Average	198 (74.7)
Difficult	39 (14.7)
Monthly income in local practice (PHP)	
4,000-10,000	36 (13.6)
8,000-15,000	43 (16.2)
12,000-20,000	76 (28.7)
16,000-20,000	47 (17.7)
> 20,000	63 (23.8)

different concepts, but studies on the relationship of age and knowledge of physiotherapy have been contradictory. In a previous study done on Japanese high school students, majority of the subjects appeared to have heard of physical therapy. The knowledge of physiotherapy was found to be significantly greater among the science and healthcare aspiring students. Hence, over half of the teen respondents were believed to have some knowledge of physiotherapy.[5] In contrast, this study suggested that majority of respondents were unaware of the clinical significance of physiotherapy and of the role of physical therapy in patient management. This finding was consistent with a similar study on Sri Lankan high school students.[6]

Area of residence also impacted on the level of awareness of people on physiotherapy.[7,8,9] In this

Table 3. Perceived work of a physical therapist.

Work aspect	Number (%)
Scope of work	
Treating patients with exercise, massage and/or modalities	94 (28.4)
Treating athletic injuries	83 (25.1)
Massaging people in their homes or spas	38 (11.5)
Treating patients with acupuncture	35 (10.6)
Treating patients through surgery	29 (8.8)
Working as gym instructor	26 (7.8)
Teaching in school	14 (4.2)
Teaching zumba lessons	12 (3.6)
Conditions treated	
Muscle / body pain	103 (29.3)
Sprain	97 (27.6)
Fractures	70 (19.9)
Stroke	38 (10.8)
Hypertension	22 (6.3)
Mental problems	10 (2.8)
Others	11 (3.1)
Equipment/methods used	
Hot / cold pack / compress	95 (31.1)
X-ray machine	67 (22.0)
Bandages	60 (19.7)
Parallel bars	40 (13.1)
Ultrasound	20 (6.6)
Injection	18 (5.9)
Microscope	5 (1.6)

Table 4. Perceived places where physical therapists work.

Place of work	Number (%)
Hospital	103 (22.9)
Sports clinic	79 (17.6)
Public health department	68 (15.1)
School	47 (10.4)
People's home	41 (9.1)
Nursing home	38 (8.4)
Doctor's office	26 (5.8)
Pediatric center	21 (4.7)
Others	27 (6.0)

Table 5. Plans of respondents after senior high school.

Plans	Number (%)
Plans after graduating from Grade 12	
Go to college	94 (83.2)
Work	10 (8.8)
Work while enrolled in college	9 (8.0)
Course to pursue (respondents going to college)	
Engineering & architecture	17 (18.1)
Tourism-related	15 (16.0)
Business-related	12 (12.8)
Computer-related	11 (11.7)
Health-related	3 (3.2)
Others	36 (38.3)

study, majority of the study subjects resided in urban areas of the National Capital Region. Given that most health services were readily available in major cities, urban dwellers might have a higher chance of being familiar with physical therapy as part of the healthcare system in the country. Nonetheless, the study subjects appeared to have very limited information on physical therapy as a potential career and profession.

Awareness of future career paths of adolescents have been known to be influenced by a myriad of factors, including significant others' perceptions and beliefs. Most of the respondents stated that their family and peers were their main sources of ideas about physical therapy, a finding also noted among Pakistani high school surdents.[10] In addition, the role of mass and social media in spreading awareness had been studied previously, and in the local setting, the influence of television and career literature was evident on the Grade 10 junior high school students.[5] This finding had been further reinforced by the Bandura Social Learning Theory which stated that children who were surrounded by influential parental figures and / or other relatives, were keen on observing and imitating their role models. If parental role models were physical therapists, or had received any form of rehabilitation physical therapy in the past, their children might be more likely to be aware of physical therapy in general.[11]

It was also apparent that majority of respondents did not know that BS Physical Therapy was a five-year course that emphasized knowledge and skills in the rehabilitation and treatment of individuals with physical disabilities, resulting from injury, illness, and ageing. They also appeared to be aware that in compliance to Philippine legislation, graduates of the degree program ought to pass the licensure examination of the Professional Regulation Commission to practice their profession.[12]

In terms of financial rewards, respondents believed that physical therapists received relatively

low monthly salaries (i.e., PhP 12,000.00 to PhP 20,000.00). Personal qualifications, such as years of clinical experience, previous work rank or appointment, degree of education and training (i.e., post-graduate courses), and geographic location and practice setting influence the monthly salary of health professionals in the Philippines.

The respondents were correct to identify human anatomy as a foundation course of physical therapy. Similarly, kinesiology and the use of exercise regimens had been properly recognized as part of the curriculum of the BS Physical Therapy program.[13] However, the misperception that physical therapists were skilled massage therapists / masseurs should be corrected. The general concept of massage therapy involved basic knowledge of gross anatomy, a competency that might be known even to the lay people. Core medical competencies of physical therapists encompassed holistic management of cardiac, stroke, burn, neurologic (i.e., cerebral palsy), and trauma (i.e., sports-related injuries) patients. Physical therapists had been trained to offer different treatment modalities, such exercise regimens (i.e., range of motion, muscle strengthening, etc.), therapeutic massage, use of other modalities (i.e., cold/heat compress/pack, electrotherapy, ultrasonography, etc.).

It was interesting also to observe that the respondents assumed the practice of physical therapists was confined to the hospital setting or sports clinics/fitness centers. Physical therapists could practice anywhere, including the community setting (i.e., home-based bedside therapy), other healthcare facilities (i.e., hospice units, home / nursing facilities, rehabilitation centers, etc.), and similar institutions (i.e., academe and research centers, industrial clinics, etc.).[14]

The study subjects correctly identified musculoskeletal disorders (i.e., muscle and body pain) as the leading medical condition addressed by physical therapists. Physical therapists have been known to engage in interventions that aimed to relieve muscle pain, involving varied forms of physical activities and training.[15] More so, physical therapists often applied of different modalities (e.g., hot moist packs / cold packs), usually utilized in sports and rehabilitation settings, during the immediate and rehabilitative phases of injury management.[16] Some study subjects also cited the x-ray machine as the equipment often requested by the physical therapist. In general, Filipino junior high school students believed exercise prescription was the most common intervention physical therapists offered to their patients. This was consistent among Pakistani pre-medical students who perceived exercise as the most common intervention used by physical therapy.[10] High-intensity resistance exercise using dumbbells was identified to play an essential role in the prevention and rehabilitation of musculoskeletal injuries and disorders.[15]

In conclusion, Filipino junior high school students appeared to have some level of knowledge on physical therapy since they had correctly identified important features of the said discipline - 1) human anatomy at the core of the curriculum; 2) requirements for passing the licensure examination prior to actual practice of physical therapy in the country; 3) musculo-skeletal disorders as the leading indication for physical therapy; and 4) use of different treatment modalities (i.e., massage, warm and cold packs) in managing various medical conditions. However, it was also obvious that BS in Physical Therapy was not a popular degree choice for the junior high school students to pursue in college, and that there were some misperceptions on the practice of physical therapy in the country.

Findings of this study may prove to be beneficial in proposing marketing strategies that will improve on the popularity of the BS Physical Therapy program as a potential college degree and / or career choice for K-12 graduates. Likewise, strengthening the partnership with the Department of Education may result in better linkages that may highlight the need to produce more physical therapists in the Philippines. Qualitative studies may be undertaken to explore reasons why the BS Physical Therapy course is not popular among junior high school students. Lastly, a wider coverage of sample may be included in the future that may also consider rural-urban differences in terms of pursuing BS Physical Therapy.

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After obtaining informed consent, the investigator distributed the questionnaire and sample instructional workbook. The respondents were asked to accomplish the questionnaire after reading the contents of the instructional workbook. The participants were given enough time to read and examine the contents of the workbook. Upon the completion of the questionnaires and retrieval from the respondents, the responses were tabulated and interpreted.

The frequency and percentages were computed for the categorical variables. For the continuous variables, the mean for each item and the weighted mean for each criterion and for recommendation were computed. The weighted means were given a qualitative description as follows: 1.00-1.49 least acceptable / recommended, 1.50-2.49 moderately acceptable / recommended, 2.50-3.49 acceptable / recommended, and 3.50-4.00 highly acceptable / recommended. The significance of sex, age, length of service and educational attainment on each of the acceptability criteria was determined using analysis of variance (ANOVA).[4]

Table 1. Demographic characteristics of 30 biochemistry faculty respondents.

Profile	Number (%)
Sex	
Male	9 (30.0)
Female	21 (70.0)
Age (yr)	
21-30	10 (33.3)
31-40	12 (40.0)
41-50	8 (26.7)
Length of Service (yr)	
1-5	5 (16.7)
6-10	5 (16.7)
11-15	8 (26.7)
16-20	8 (26.7)
≥ 21	4 (13.3)
Highest educational attainment	
MA/MS Graduate	14 (46.7)
With PhD/EdD Units	12 (40.0)
PhD/EdD Graduate	4 (13.3)

Results

Thirty faculty from two campuses were included in the study. Majority of them were women, 40 years old or younger, and had been teaching for 10-20 years. Almost half of respondents were holders of master's degrees and more than a third were working on or had doctorate degrees. The respondents' characteristics are shown in Table 1.

The respondents level of acceptance in terms of the learning objectives was high with a grand weighted mean (GWM) of 3.55, as shown in Table 2. Content (GWM = 3.38), usefulness (GWM = 3.37), clarity (GWM = 3.33), presentation (GWM = 3.46), evaluation (GWM = 3.29), and language and style (GWM = 3.45) were rated as acceptable as seen in Tables 3 to 8. None of the individual items under

Table 2. Respondents' assessment of the level of acceptability of the proposed instructional workbook in terms of learning outcomes.

Criteria	WM	QD
1. Institutional learning outcome provided in each lesson can change students' behavior	3.57	HA
2. Learning outcome is in line with the mission, goals and learning outcome of science both departmental and institutional	3.64	HA
3. Consists of learning opportunities and institutional	3.60	HA
4. Appropriate and can be achieved within time-frame	3.33	A
5. Complex and sufficient to improve students' performance and achievements.	3.60	HA
Grand Weighted Mean	3.55	HA

Legend: WM - weighted mean; QD - qualitative description; HA - highly acceptable; A - acceptable

each criterion received a score lower than 3. The items on "utilizing diagrams to motivate students" under presentation and on "providing scientifically-arranged ideas to help students work independently" under language and style received the highest mean score from the respondents at 3.73 (Tables 6 & 8).

Among the respondents' demographic characteristics, age, length of service and educational attainment had significant impact on the acceptability of the proposed instructional workbook in terms of all seven criteria, except for age which was not significant for language and style, as shown in Table 9. The same table also shows that sex was significant only for usefulness and clarity. The respondents' mean score on whether or not they would recommend the proposed instructional workbook to their colleagues was 3.17, equivalent to a rating of "recommended".

Table 3. Respondents' assessment of the level of acceptability of the proposed instructional workbook in terms of content.

Criteria	WM	QD
1. Sufficient and complete covering the topics	3.43	A
2. Provides learning opportunities and experiences to improve students' knowledge, understanding and skills,	3.47	A
3. Provides appropriate and relevant diagrams to enhance students' understanding and problem-solving skills	3.30	A
4. Provides variety of teaching methodologies and techniques to suit individual needs.	3.47	A
5. Deepens students' understanding of concepts and principles so that they can apply it in their daily living	3.17	A
6. Diagrams utilized are sufficient, properly presented/labeled, and relevant to the lesson.	3.43	A
Grand Weighted Mean	3.38	A

Legend: WM - weighted mean; QD - qualitative description; HA - highly acceptable; A - acceptable

Table 4. Respondents' assessment of the level of acceptability of the proposed instructional workbook in terms of usefulness.

Criteria	WM	QD
1. Very useful in developing students':		
1.1. Exploration of concepts.	3.47	A
1.2. Understanding of laws and principles.	3.60	HA
1.3. Skills in applying the learned concepts, laws and principles.	3.30	A
2. Improves students' achievements.	3.30	A
3. Widens and deepens students' abilities to explain and interpret results.	3.43	A
4. Enhances meaningful students' experiences	3.13	A
5. Various teaching strategies are applied to meet students' needs and level of capabilities.	3.43	A
Grand Weighted Mean	3.37	A

Legend: WM - weighted mean; QD - qualitative description; HA - highly acceptable; A - acceptable

Table 5. Respondents' assessment of the level of acceptability of the proposed instructional workbook in terms of clarity.

Criteria	WM	QD
1. Clear presentation of concepts, laws and principles needed by the students	3.17	A
2. Activities are presented in a simple manner so that students can perform and work independently	3.30	A
3. Language used is clear, brief and within the level of understanding of students	3.30	A
4. Diagrams utilized are simple and appropriate to the concepts and principles discussed/asked	3.47	A
5. Diagrams provide a clear discussion and application of concepts and principles	3.47	A
6. Instructional workbook and content complement each other, thus developing students' self-confidence and skills	3.30	A
Grand Weighted Mean	3.33	A

Legend: WM - weighted mean; QD - qualitative description; A - acceptable

Table 6. Respondents' assessment of the level of acceptability of the proposed instructional workbook in terms of presentation.

Criteria	WM	QD
1. Presented in a sequential manner according to the course syllabus of Biochemistry I	3.47	A
2. Well-organized that teachers and students can use it properly and independently	3.57	HA
3. Parts consist of lesson title, learning outcome, introduction, content, evaluation and application	3.30	A
4. Diagrams utilized can motivate students' interests, curiosity, and awareness	3.73	HA
5. Diagrams present the concepts and principles that guide students to solve problems accurately	3.43	A
6. Simple and clear presentation of the application of laws and principles	3.27	A
Grand Weighted Mean	3.46	A

Legend: WM - weighted mean; QD - qualitative description; HA - highly acceptable; A - acceptable

Table 7. Respondents' assessment on the level of acceptability of the proposed instructional workbook in terms of evaluation.

Criteria	WM	QD
1. Sufficient to determine if transfer of learning occurs	3.33	A
2. Directions, instructions and problem statements are simple and easy to follow	3.30	A
3. Complete to determine students' acquisition of:		
3.1. Knowledge of concepts	3.30	A
3.2. Understanding of laws	3.17	A
3.3. Skills in applying principles	3.17	A
4. Relevant to the topics being discussed	3.27	A
5. Provision of diagrams to make students fully understand how concepts and principles can be applied	3.47	A
Grand Weighted Mean	3.29	A

Legend: WM - weighted mean; QD - qualitative description; A - acceptable

Table 8. Respondents' assessment of the level of acceptability of the proposed instructional workbook in terms of language and style.

Criteria	WM	QD
1. Contents are clear, brief and simple.	3.60	HA
2. Words, sentences, statements used are within the level of comprehension of the students.	3.57	HA
3. Diagrams are systematically designed and presented in a simple manner.	3.27	A
4. Format and diagrams attract students' interests and awareness.	3.40	A
5. Simple and sequential presentation of concepts, laws and principles.	3.13	A
6. Provides scientifically-arranged ideas that help students work independently, developing their work with accuracy and self-confidence.	3.73	HA
Grand Weighted Mean	3.45	A

Legend: WM - weighted mean; QD - qualitative description; HA - highly acceptable; A - acceptable

Table 9. Comparison of the respondents' assessment on the level of acceptability of the proposed instructional workbook based on demographic characteristics.

	Profile			
Criteria	Sex	Age	Length of service	Highest educational attainment
Learning outcome	0.386	0.003	0.000	0.000
Content	0.935	0.001	0.000	0.000
Usefulness	0.000	0.000	0.047	0.000
Clarity	0.003	0.000	0.000	0.000
Presentation	0.237	0.000	0.034	0.000
Evaluation	0.162	0.000	0.000	0.000
Language & style	0.620	0.849	0.000	0.000

Significant at $p<0.05$

Discussion

The respondents rated the proposed instructional workbook as acceptable in six criteria and highly acceptable in the other criterion (learning objectives). Based on their assessment, the workbook is recommended. Age, length of service and educational attainment were demographic characteristics that significantly affected acceptability.

The results show that the faculty's experience, as reflected by age and length of service, is a major factor in determining acceptability. It is postulated the more senior faculty have mastered the craft of teaching biochemistry and know what techniques and approaches work. The figures further show that sex is not a major factor in acceptability as it was significant only in "usefulness" and "clarity" but not in the other five criteria.

Based on the summary findings retrieved from the study, the researcher has concluded that the proposed instructional workbook can be used as an instructional guide for students elsewhere in the country or beyond. The researcher has also concluded that the respondents accepted the use of the proposed instructional workbook when it was evaluated in terms of objectives, content, usefulness, clarity, presentation, evaluation, language and style. Topics that were evaluated by the respndents include the cell, carbohydrates and proteins.

Based on the conclusions drawn from the study, the researcher recommends the following:

1. Periodic revisions on the content of the instructional workbook should be made to update the procedural design and methodology of the instructional workbook.

2. The proposed instructional workbook in biochemistry that covers the topics of the cell, carbohydrates, and proteins is recommended for use in the teaching of biochemistry in Libya.

3. Since there was a significant difference on the level of acceptability in terms of the demographic profile specifically on the areas of length of service and highest educational attainment, continuous studies and training to gain more knowledge and skills among the faculty members should be encouraged.

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Declaration of conflict of interest

The author declares that there is no conflict of interest herewith with regards to the publication of the study.

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Spirituality and self-efficacy among caregivers of patients with terminal illness

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Abstract

Introduction This study was conducted to determine the level of spirituality in relation to self-efficacy among relatives and watchers taking care of terminally-ill cancer patients admitted at the University of East Ramon Magsaysay Memorial Medical Center, Inc.

Methods The study utilized a descriptive correlational design with a purposive sampling method. Outcome measures included survey questionnaires, namely O'Brien's Level of Spirituality Questionnaire and Bandura's Self-Efficacy Questionnaire. Relatives and other watchers of patients classified as category 4 (terminally-ill) were included. Spearman-Rho was used in analyzing the data gathered.

Results The findings revealed a negative moderate relationship between self-efficacy and spiritual contentment. Additionally, very weak relationships were observed between self-efficacy and religious practices as well as self-efficacy and personal faith.

Conclusion There is no significant relationship between the level of spirituality and self-efficacy of the support group of terminally-ill patients. Analysis of data collected proved that a change in one variable does not have significant impact on the other.

Key words: Spirituality, self-efficacy, terminal illness, support group

According to Barager, a person's attitude toward his illness has a huge impact, not just on what he can achieve, but on his total quality of life. A positive or negative outlook can affect his disease process by altering the patient's compliance to treatment.[1] The patient's support group or significant others have a critical role to play. They can make or break a patient's outlook of his illness. Teleghani showed that patients backed up or encouraged by a support group enjoyed a higher quality of life compared to others.[2]

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A person's level of spirituality and self-efficacy are vital to a person's well-being and judgement. Spirituality, according to Merriam Webster Online, is the quality or state of being spiritual, also the force within a person that is believed to give the body life, energy, and power.[3] Krentzman stated that spirituality is about seeking a meaningful connection with something bigger than oneself, which can result in positive emotions, such as peace, awe, contentment, gratitude, and acceptance.[4] On the other hand, Bandura defined self-efficacy as a person's belief in his own ability to succeed in a particular situation. It is what an individual believes he or she can accomplish on his or her own under certain circumstances.[5]

The study sought to determine the relationship between the level of spirituality and self-efficacy of the caregiver support group of terminally-ill patients

admitted in the UERM Memorial Medical Center. Specifically, it aimed to determine 1) the level of spirituality of the caregiver support group in terms of personal faith, religious practice and spiritual contentment and 2) the level of self-efficacy of the caregiver support group.

Methods

The investigators surveyed the caregiver support group of terminally-ill patients confined at the UERM Memorial Medical Center using two questionnaires, the Spirituality Assessment Scale and the Perceived Collective Family Efficacy Tool. The mean scores of the Spirituality Assessment Scale and the Perceived Collective Family Efficacy Tool were correlated to determine the relationship of the support group's level of spirituality with self-efficacy. The study was approved by the Ethics Review Committee of the Medical Center and coordinated with the hospital administration.

Family members of patients confined in the hospital were recruited by purposive sampling. They were included in the study if they were immediate family members at least 18 years old or caring for a patient who had been terminally-ill for at least five years and had given an informed consent. Those who had been caring for the patient for less than a month were excluded. The sample size of 21 respondents was computed based on a standard deviation = 1.7 and alpha = 0.05.6

The instruments used were the Spiritual Assessment Scale (SAS) and the Perceived Collective Family Efficacy Tool (PCFET). The SAS is a 21-item questionnaire that covers personal faith, religious practice and spiritual contentment. It utilizes a 5-point Likert type scale - strongly agree (SA = 5), agree (A = 4), uncertain (U = 3), disagree (D = 2) and strongly disagree (SD = 1). Seven items on personal faith touch on belief in a God who takes care of all creatures; peace, confidence, strength and comfort, trust in God; and a positive self-image. Religious practice consists of seven items concerning belonging to a church or faith group; being strengthened, satisfied, supported, comforted by the church or group; and relationship and communication with God. The items on spiritual contentment involve pain, distance from God, fear of unforgiveness or that God may not take care of one's needs, anger, loss of God's love, and despair.[7] The instrument has an overall alpha coefficient of 0.92.[8] The highest possible score for each subscale is 35 points and 105 overall; a high score is interpreted as a higher level of spirituality.

The Perceived Collective Family Efficacy Tool is a 20-item questionnaire covering leisure time, decision-making, preventing and resolving conflicts, sharing household responsibilities, supporting, helping, trusting, close ties, traditions and other family concerns. Each item is scored from 0 (cannot do at all) to 100 (highly certain can do) points in intervals of 10 points. A higher score is interpreted as a higher general self-efficacy.[9]

The investigators went to the different wards, informed the head nurses about their objective, and then selected potential respondents. The investigators then obtained an informed consent from those willing to be part of the study. The respondents were asked to answer two sets of questionnaires. The researchers collected the answered questionnaires and checked them for completeness.

Descriptive statistics for the participants' sociodemographic characteristics as well as mean scores for the SAS and PCFET were computed. The overall spirituality, personal faith, religious practices and spiritual contentment were correlated with self-efficacy using Spearman's rho coefficient.

Results

Sixty-three persons taking care of cancer patients confined in the hospital participated in the study. More than half were women and more than 80% were adults less than 50 years old. Their mean age was around 33 years. Around 60% were Catholics. The details are shown in Table 1.

The results show that the personal faith aspect of spirituality has a weak relationship with self-efficacy (r = 0.126). The domain religious practices has a weak inverse relationship with self-efficacy (r = -0.26). Spiritual contentment has a moderate inverse relationship with self-efficacy (r = -0.58). The details are shown in Table 2.

Discussion

Many of the respondents were in their 30s, consistent with other findings that older workers may not participate in learning and development activities as much as younger workers.[9] This paper explores an

Table 1. Demographic characteristics of respondents (N = 63).

Characteristic	Frequency (%)
Sex	
Female	36 (57.1)
Male	27 (42.9)
Age	
18-27	24 (38.1)
28-37	20 (31.7)
38-47	9 (14.3)
48-57	5 (7.9)
58-67	3 (4.8)
≥ 68	2 (3.2)
Religion	
Roman Catholic	38 (60.3)
Christian	10 (15.9)
Iglesia ni Cristo	10 (15.9)
Others	5 (7.9)

Table 2. Relationship of domains of spirituality with self-efficacy.

	Mean ± SD	Spearman Rho
Self-efficacy	72.1 ± 3.10	0.126
Personal faith	4.2 ± 0.22	
Self-efficacy	72.1 ± 3.10	-0.26
Religious practices	4.2 ± 0.32	
Self-efficacy	72.1 ± 3.10	-0.58
Spiritual contentment	3.8 ± 0.50	

important and under-recognized factor that may contribute to this age effect: a decline in self-confidence (or self-efficacy) for career-relevant learning and skill development with age.

Dorahy and Lewis examined cross-cultural groups and the intersection of religious beliefs and life satisfaction and found that for men, religion seems to make a greater difference in life satisfaction than for women, although women may express greater religiosity.[10] This may be an explanation for the results of the study.

The results are similar to the findings of Omu that religious faith was not related to either life satisfaction or self-efficacy.[11] The study failed to show any significant relationship between religious faith and self-efficacy or life satisfaction in female stroke patients living in Kuwait. However, results from patient and health professional interviews identified religious beliefs as playing an important role in recovery, behavior during rehabilitation and in interaction with health professionals. The said study highlights the importance of taking into consideration religious and cultural influences during the rehabilitation of stroke patients in Kuwait. It should be noted that majority of the present study's patients and respondents were Catholics.

Based on Sister Callista Roy's Adaptation Model of Nursing, humans are holistic beings that are in constant interaction with their environment.[12] Humans use a system of adaptation, both innate and acquired, to respond to the environmental stimuli they experience. Human systems can be individuals or groups, such as families, organizations, and the whole global community. The integrity and organization of the self may be threatened by a variety of assaults. They may involve the physical self, through trauma or debilitating, disfiguring or life-threatening disease, which is what the patients of the present study's respondents are afflicted with. This has been identified as the processes in which people adjust to these negative or threatening events. Adegbola reported that self-efficacy was positively related to spirituality.[13] Reicks, Mills and Henry found out that spiritual practices such as prayer and reading scripture enhanced confidence to perform behaviors that enabled weight loss, and concluded that, for some, spirituality contributed to self-efficacy and attainment of goals.[14] Self-efficacy has frequently been suggested as an important factor in successful management of chronic illness and can give direction to relevant health promotion strategies, though this was not seen in the present study.

Results showed that there is no significant relationship between the level of spirituality in terms of personal faith, religious practices, and spiritual contentment, and self-efficacy of the caregiver support group of terminally-ill patients. Analysis of data collected proved that an increase or decrease in one variable does not have much impact on the other. From the findings above, recommendations for future researchers include the extension of the study to different centers or hospitals. Additionally, future investigators are encouraged to conduct a study

regarding the level of spirituality and self-efficacy of the support group of terminally-ill patients with specific diseases. The investigators would also like to recommend conducting a study focused on the support group of pediatric patients to know whether the age of the patient has an impact on the support group's level of spirituality and self-efficacy.

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Antibiotics versus no antibiotic therapy for uncomplicated sigmoid diverticulitis: A meta-analysis

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Abstract

Introduction Antibiotics have been used customarily in the treatment of uncomplicated diverticulitis since their introduction and have become the standard of care. The aim of this study is to compare the effectiveness of antibiotic therapy versus no antibiotic therapy in the treatment of uncomplicated sigmoid diverticulitis.

Methods An electronic search for randomized controlled trials comparing antibiotics versus no antibiotic therapy for uncomplicated diverticulitis was conducted. The outcomes considered were associated morbidity (abscess formation and sigmoid perforation); need for sigmoid colon resection, and recurrence of diverticulitis. The included studies were evaluated for risk of bias. Meta-analysis with Forest plot was performed using Review Manager Version 5.3.

Results Two trials, consisting of 1,151 subjects, were included in the meta-analysis. There was no difference in the risk of sigmoid perforation (RR 1.02, 95% CI 0.30, 3.49). Abscess formation and incidence of sigmoid resection were lower in the antibiotics groups (RR 2.24, 95% CI 0.51, 9.95 and RR 1.59, 95% CI 0.75, 3.36, respectively) but the differences were not significant. There was no difference in the recurrence of diverticulitis (RR 1.05, 95% CI 0.74, 1.48) between the two groups.

Conclusion There is no definite advantage in giving antibiotics to patients with uncomplicated diverticulitis. Not giving antibiotics may be an acceptable treatment option for patients with acute uncomplicated sigmoid diverticulitis.

Key words: diverticular disease, uncomplicated diverticulitis, conservative management, antibiotics, treatment

Diverticulitis refers to inflammation and infection associated with a diverticulum in the bowel. The sigmoid colon is the most common site.[1,2] The pathophysiologic mechanism underlying sigmoid diverticulitis is not well-understood. However, the long-held belief that colonic diverticulitis is caused by microperforation and bacterial infection has been challenged by the concept that diverticulitis may be a primary inflammatory process.[3]

Uncomplicated sigmoid diverticulitis is the presence of inflamed sigmoid colon diverticula in the absence of complications such as perforation leading to peritonitis, fistula formation, obstruction due to stricture, and/or bleeding. It is usually

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characterized by an acute onset of left lower quadrant abdominal pain and tenderness. Computed tomography findings include the presence of colonic diverticula with associated pericolic soft tissue stranding, colonic wall thickening, and/or phlegmon formation.[1]

Most patients with uncomplicated diverticulitis in the sigmoid colon will respond to conservative treatment in an out-patient setting.[1,2] Conservative treatment of mild colonic diverticulitis typically includes careful observation while placing the patient on a low-residue diet with broad-spectrum oral antibiotics.[2] In a small number of patients with a more serious presentation such as severe abdominal pain, tenderness, fever, and leukocytosis, in-hospital treatment with bowel rest and parenteral antibiotics is done.[2] The majority of patients with uncomplicated sigmoid diverticulitis improves with these conservative measures and recovers without surgery.[2,4]

Antibiotics have been used customarily in the treatment of uncomplicated left-sided colonic diverticulitis and have become the standard of care. Recently, a Cochrane database review found contradictory results between two randomized controlled trials with regard to the use of antibiotics in the treatment of uncomplicated sigmoid diverticulitis.[5] The DIABOLO trial investigated the cost-effectiveness of treatment with or without antibiotics for uncomplicated acute sigmoid diverticulitis showed no significant difference in full recovery between the two strategies.[6] On the other hand, the AVOD study group showed antibiotic treatment neither accelerates recovery nor prevents complications or recurrence of diverticulitis.[7]

The aim of our study is to compare the effectiveness of antibiotic therapy versus no antibiotic therapy in the treatment of uncomplicated sigmoid diverticulitis. Specifically, it aims to compare the incidence of morbidity in terms of perforation and abscess formation, sigmoid resection, and recurrence. The study also compares the length of hospital stay and clinical signs between the two treatment strategies.

Methods

Trials that were included in the study are those comparing antibiotic therapy versus no antibiotic therapy for uncomplicated sigmoid diverticulitis published in English. Randomized controlled trials wherein the participants were diagnosed by CT scan to be stages 1a and 1b according to the Modified Hinchey's classification or "mild" diverticulitis according to Ambrosetti's criteria were included. The trials should have determined at least one of the following outcomes: morbidity, specifically sigmoid perforation and abscess formation; incidence of surgical resection (sigmoidectomy or partial colectomy); and recurrence. Trials that also looked into length of hospital stay and abdominal pain and tenderness were considered.

All randomized clinical trials comparing antibiotics versus no antibiotic therapy in patients diagnosed with uncomplicated sigmoid diverticulitis were identified by conducting an electronic search of the databases from Cochrane Library, PubMed and Google Scholar using the following keywords: diverticular disease, uncomplicated diverticulitis, sigmoid diverticulitis, conservative management, antibiotics, treatment. A comprehensive hand search of reference lists of published articles and review articles was performed to ensure inclusion of all possible studies and to exclude duplicates. Included were articles published in English up to May 2017. Review articles, non-randomized trials, retrospective analyses, and abstracts were not considered.

All potential trials were screened according to the criteria specified in the research protocol. Three reviewers extracted data from each publication. The third reviewer served as the arbiter who resolved all discrepancies. The quality of included studies was assessed independently by three reviewers using the Cochrane Handbook for Systematic Reviews of Interventions criteria: random sequence generation, allocation concealment, blinding of the patient and the observer, blinding of outcome assessment, incomplete outcome data, and selective outcome reporting. The main comparison was stratified according to morbidity, incidence of surgery, recurrence and length of hospital stay.

The relative risk or risk ratio (RR) was the primary measure of treatment effect or adverse events, and 95 per cent confidence intervals (CI) for RR were calculated. Heterogeneity was assessed by Q-square (v2) and I-square statistics (I^2).[8,9] The I^2 statistic indicated the degree of between-study or interstudy variability as opposed to within-study or intra-study variability. An I^2 value greater than 50% was considered as substantial heterogeneity.[8,9] Studies were analyzed using the fixed-effects model; when heterogeneity was significant, the random-effects

characterized by an acute onset of left lower quadrant abdominal pain and tenderness. Computed tomography findings include the presence of colonic diverticula with associated pericolic soft tissue stranding, colonic wall thickening, and/or phlegmon formation.[1]

Most patients with uncomplicated diverticulitis in the sigmoid colon will respond to conservative treatment in an out-patient setting.[1,2] Conservative treatment of mild colonic diverticulitis typically includes careful observation while placing the patient on a low-residue diet with broad-spectrum oral antibiotics.[2] In a small number of patients with a more serious presentation such as severe abdominal pain, tenderness, fever, and leukocytosis, in-hospital treatment with bowel rest and parenteral antibiotics is done.[2] The majority of patients with uncomplicated sigmoid diverticulitis improves with these conservative measures and recovers without surgery.[2,4]

Antibiotics have been used customarily in the treatment of uncomplicated left-sided colonic diverticulitis and have become the standard of care. Recently, a Cochrane database review found contradictory results between two randomized controlled trials with regard to the use of antibiotics in the treatment of uncomplicated sigmoid diverticulitis.[5] The DIABOLO trial investigated the cost-effectiveness of treatment with or without antibiotics for uncomplicated acute sigmoid diverticulitis showed no significant difference in full recovery between the two strategies.[6] On the other hand, the AVOD study group showed antibiotic treatment neither accelerates recovery nor prevents complications or recurrence of diverticulitis.[7]

The aim of our study is to compare the effectiveness of antibiotic therapy versus no antibiotic therapy in the treatment of uncomplicated sigmoid diverticulitis. Specifically, it aims to compare the incidence of morbidity in terms of perforation and abscess formation, sigmoid resection, and recurrence. The study also compares the length of hospital stay and clinical signs between the two treatment strategies.

Methods

Trials that were included in the study are those comparing antibiotic therapy versus no antibiotic therapy for uncomplicated sigmoid diverticulitis published in English. Randomized controlled trials wherein the participants were diagnosed by CT scan to be stages 1a and 1b according to the Modified Hinchey's classification or "mild" diverticulitis according to Ambrosetti's criteria were included. The trials should have determined at least one of the following outcomes: morbidity, specifically sigmoid perforation and abscess formation; incidence of surgical resection (sigmoidectomy or partial colectomy); and recurrence. Trials that also looked into length of hospital stay and abdominal pain and tenderness were considered.

All randomized clinical trials comparing antibiotics versus no antibiotic therapy in patients diagnosed with uncomplicated sigmoid diverticulitis were identified by conducting an electronic search of the databases from Cochrane Library, PubMed and Google Scholar using the following keywords: diverticular disease, uncomplicated diverticulitis, sigmoid diverticulitis, conservative management, antibiotics, treatment. A comprehensive hand search of reference lists of published articles and review articles was performed to ensure inclusion of all possible studies and to exclude duplicates. Included were articles published in English up to May 2017. Review articles, non-randomized trials, retrospective analyses, and abstracts were not considered.

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model described by DerSimonian and Laird was used.[9] Meta-analysis using Forest plots was performed with Review Manager Version 5.3.

Results

The search strategy resulted in 491 studies from the online databases. After excluding duplicates and articles that did not meet the inclusion criteria, seven full texts were reviewed for eligibility. Five articles were excluded because they were not randomized trials, leaving two for inclusion in the meta-analysis as seen in Figure 1.

Two trials were included in the meta-analysis and their characteristics are summarized in Table 1. The two studies included a total of 1,151 participants - 571 in the no antibiotic group and 580 in the antibiotic group. The AVOD and DIABOLO studies followed up their patients for 1 and 2 years, respectively. Both studies satisfied the criteria for assessment except for blinding of patients and personnel. Assessment of quality according to the Cochrane Collaboration's tool for assessing risk of bias summary for RCTs is reported in Figure 2.

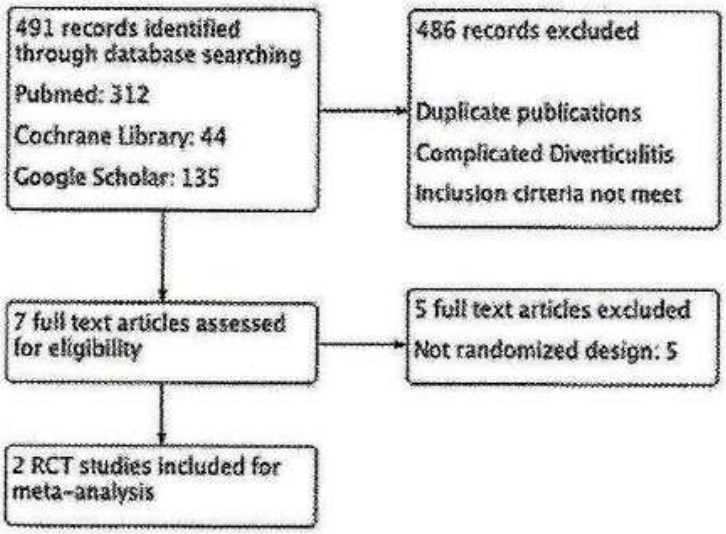

Figure 1. Study selection flowchart.

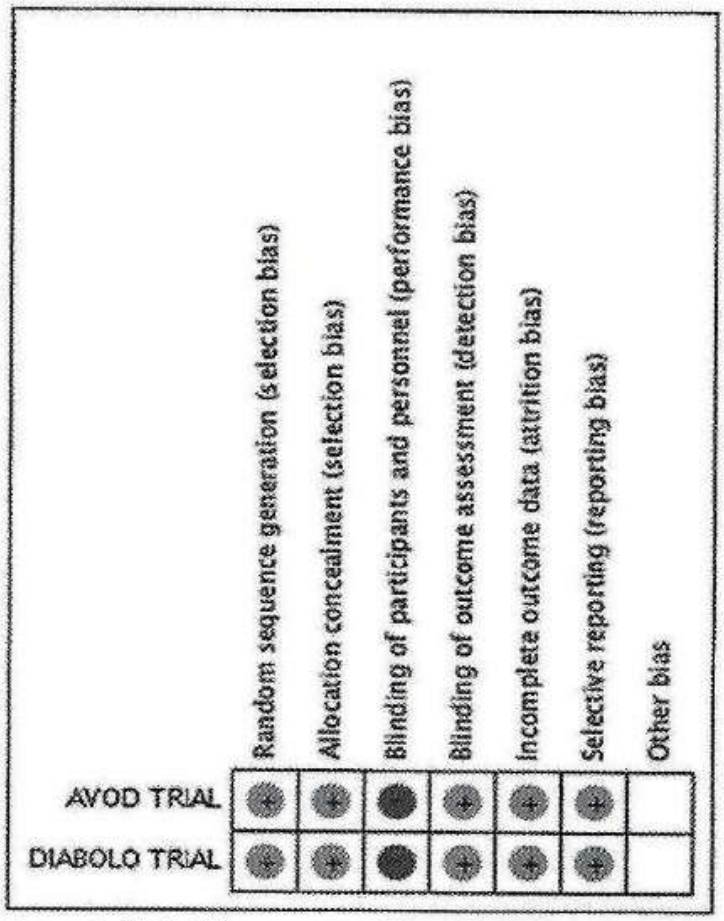

Figure 2. Risk of bias summary. (Gray - low risk of bias, Black - high risk, white - unclear)

Table 1. Summary of included studies.

Characteristic	AVOD trial, 2012[6]	DIABOLO trial, 2016[7]
Population	623	528
Follow up (months)	12	24
Antibiotics used	Cefuroxime / cefotaxime plus metronidazole, or carbapenem, or piperacillin-tazobactam, shifted to oral ciprofloxacin/ cefadroxil plus metronidazole	Amoxycillin-clavulanic acid IV shifted to oral
Outcomes	Complications (abscess formation, perforation), emergency surgery, hospital stay, recurrence	Recovery, days spent outside hospital (6 months), readmissions, complicated diverticulitis (abscess, perforation, obstruction/stricture, bleeding, fistula), ongoing diverticulitis, recurrence, need for resection/ surgery, other adverse events, mortality

Figure 3 demonstrates the incidence of sigmoid perforation between no antibiotics versus with antibiotics showing no statistical difference (overall effect P = 0.98). The incidence was 5 out of 566 subjects (0.88%) for the no antibiotics group versus 5 out of 575 subjects (0.86%) for the antibiotics group. The difference is not significant. As seen in Figure 4, abscess formation was seen in 5 out of 566 subjects (0.9%) for the no antibiotics group compared with 2 out of 578 subjects for the antibiotics group (0.3%). The overall risk ratio was 2.24 (95% CI, 0.51-9.95) and tends to favor the antibiotics group but is inconclusive.

The sigmoid was resected in 17 out of 554 subjects (3.0%) in the no antibiotics versus 11 out of 569 subjects (1.9%) in the antibiotics group. The risk ratio of 1.59 (95% tends to favor with antibiotics group but is inconclusive as seen in Figure 5. There was recurrence in 56 out of 552 subjects (10.1%) in the no antibiotics group compared with 54 out of 558 subjects (9.7%) in the antibiotics group. The overall risk ratio was 1.05 (95% CI, 0.74-1.48), indicating no statistical difference in recurrence between the antibiotics and no antibiotics group (Figure 6).

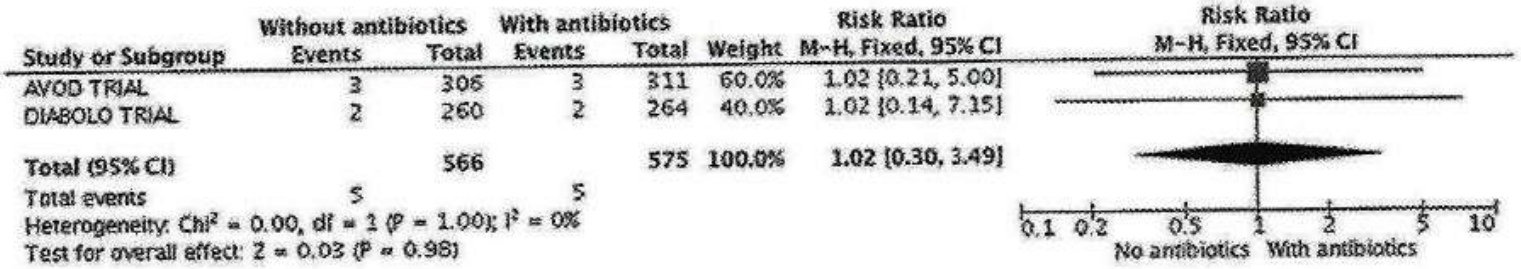

Figure 3. Comparison of sigmoid perforation between antibiotic and no antibiotic groups.

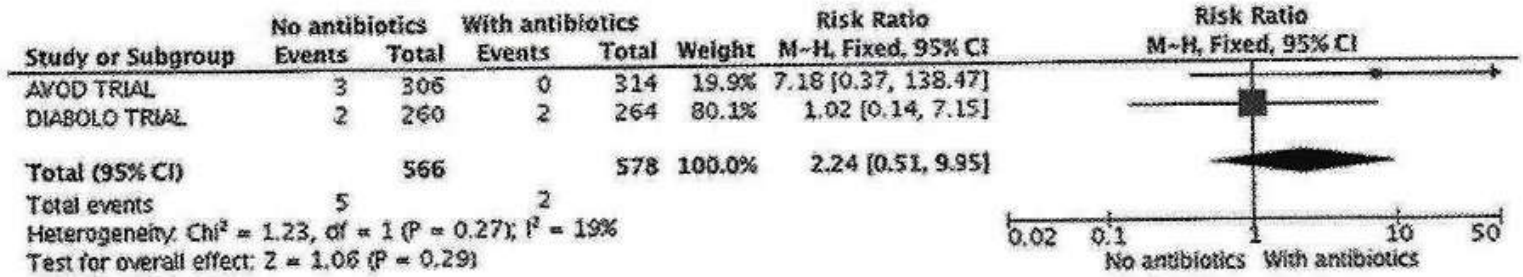

Figure 4. Comparison of incidence of abscess formation between antibiotic and no antibiotic groups.

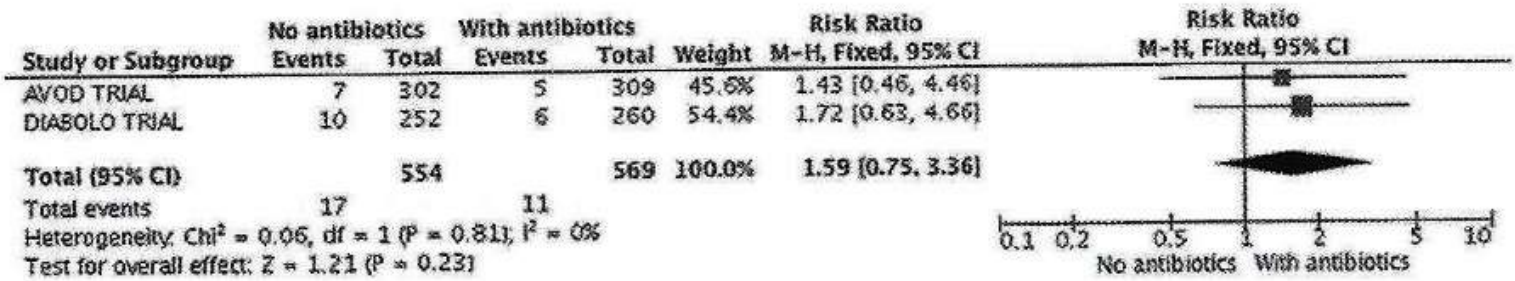

Figure 5. Comparison of incidence of sigmoid resection between antibiotic and no antibiotic groups.

The median length of hospital stay in both groups was comparable. In the AVOD trial, median length of hospital stay was 3 days in the no antibiotics group versus 3 days in the antibiotics group.[7] Whereas in the DIABOLO trial, results demonstrated median length of hospital stay of 2 days in the no antibiotic group versus 3 days in the antibiotics group.[6] Clinical bedside signs, such as abdominal pain, measured by VAS and tenderness on abdominal palpation at admission, did not differ between the groups.

Discussion

In this meta-analysis, treatment strategies using antibiotics versus no antibiotic therapy for uncomplicated sigmoid diverticulitis demonstrated no statistical difference between the two groups in terms of complications such as sigmoid perforation and abscess formation; incidence of sigmoid colon resection, and recurrence of diverticulitis. The risk ratio for patients who had undergone sigmoid colon resection (RR 1.59, 95% CI 0.75, 3.36) and patients who had abscess formation (RR 2.24, 95% CI 0.51, 9.95) tends to favor the antibiotic group, but is inconclusive.

Guidelines regarding treatment strategies for acute uncomplicated sigmoid diverticulitis have remained unchanged. According to Chabok, the recommendations for giving antibiotic therapy are based on tradition and expert opinions, and not on evidence derived from controlled clinical trials.[7] Current guidelines have stated bowel rest or intake of oral fluids and a 7 to 10-day regimen of broad-spectrum antibiotics is recommended in patients with uncomplicated sigmoid diverticulitis.[10-12] Meanwhile, the likelihood that treatment of uncomplicated sigmoid diverticulitis may not require antibiotics was described and has been raised in literature.[13] Two observational studies have also indicated that antibiotic therapy for uncomplicated sigmoid diverticulitis showed no benefit.[14,15] Furthermore, two more retrospective cohort studies have indicated that a no-antibiotic policy for acute uncomplicated diverticulitis is feasible and safe.[16,17]

The rationale behind treating an episode of uncomplicated left-sided colonic or sigmoid diverticulitis with antibiotics lies in the fact that it has long been believed that all forms of diverticulitis are the result of a colonic microperforation caused by inspissated stool in a diverticulum. However, an overlap between diverticulitis and inflammatory bowel disease has long been recognized, and recent studies have postulated that all diverticular disease could be a form of inflammatory bowel disease.[18] Altering the inflammatory response in cases of mild diverticulitis may be a more logical step than giving antibiotics.[5]

Antibiotic resistance has become a worldwide problem, and the use of antibiotics has other potential side effects such as nausea and vomiting, development of *Clostridium difficile* colitis, and fatal allergic reactions, among others.[5] The possible development of such symptoms provides another important reason for reducing the frequent use of antibiotics in these patients.[7] It could also be concluded that the risk of adverse effects and high costs warrant selective use whenever possible.[14]

A limitation of this study is the need for more randomized controlled studies comparing the use of antibiotics versus no antibiotics for acute uncomplicated sigmoid diverticulitis.

In this study, treatment strategies using antibiotics versus no antibiotic therapy for uncomplicated sigmoid diverticulitis demonstrated comparable results in terms of complications (sigmoid perforation, abscess formation), incidence of sigmoid colon resection, and recurrence. The risk ratio for patients who had undergone sigmoid colon resection and patients who had abscess formations tends to favor the antibiotic group, but is still inconclusive. Thus, there is no definite advantage in giving antibiotics to patients with uncomplicated diverticulitis. From these results, it may be postulated that not giving antibiotics may be an acceptable treatment option for patients with acute uncomplicated sigmoid diverticulitis.

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Primary serous papillary carcinoma arising from the omentum with metastasis to the parametrium and bilateral ovarian and fallopian tube serosal surface: A case report*

Francia Victoria A. de los Reyes, MD and Janet Lim-Dy, MD

Abstract

Introduction Primary peritoneal serous carcinoma is a rare, malignant, epithelial tumor arising from the peritoneum and associated tissues, that presents commonly with diffuse peritoneal involvement and ascites. Carcinomas that morphologically resemble papillary serous carcinoma of the ovary, with uninvolved or minimally involved ovaries, with the lesion of the peritoneum larger than other primary ovarian lesions, and with no other identifiable primary tumor, are categorized under such. The aim of this report is to contribute to the fund of knowledge pertinent to this rare lesion with a relatively poor prognosis.

Case Summary This report describes a case of primary carcinoma of the omentum with papillary configuration in a 53-year-old woman who presented with abdominal distention. She had no prior surgical procedure other than bilateral tubal ligation. Immunohistochemistry studies support the diagnosis and Ki67 index and p53 expression complements the high-grade morphology. The immunohistochemistry of the tumor is compared with the immunohistochemistry of other reported cases.

Conclusion This report contributes to the fund of knowledge of the clinical presentation, morphologic findings, and immunohistochemistry profile pertinent to this rare lesion for better understanding, leading to prompt diagnosis and improved quality of care.

Key words: Primary peritoneal serous carcinoma, omentum, serous carcinoma, malignant serous neoplasm

Primary serous carcinoma of the peritoneum is a rare malignancy with an incidence of 6.78 cases per 1,000,000 individuals, presenting commonly with diffuse peritoneal involvement and ascites.[1,2] First described by Swerdlow in 1959 as mesothelioma of the pelvic peritoneum, diagnosis of this entity is made for tumors that are histologically similar to serous carcinomas of the ovary, and requires that the presence of another primary tumor be excluded. Although this tumor's clinical behavior, histologic appearance, and treatment are similar to serous ovarian cancer stage III, evidence indicating a worse prognosis for the primary peritoneal lesion with a median survival rate of 12-25 months has been reported, making proper differentiation of the tumor with the ovarian counterpart is necessary.[3]

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* One of the top 15 posters among 55 poster presentation cases in the 11th Annual Meeting of the Asia Pacific Society for Molecular Immunohistology and the 3rd Asia-Australasia Pulmonary Pathology Society Meeting, December 10, 2016, Taipei, Taiwan.

The Case

The patient is a 53-year-old woman who experienced increasing abdominal girth associated with a feeling of distention, easy fatigability, decrease in appetite, and weight loss of one month. Her only surgical procedure was a bilateral tubal ligation 28 years prior. Imaging studies showed a pelvo-abdominal mass with omental involvement that was interpreted as an ovarian carcinoma with omental metastases. The initial serum CA-125 was 487 u/mL preoperatively. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and omentectomy.

Gross findings (Figure 1)

The gross specimen was received in 10% phosphate buffered formaldehyde and consisted of the uterus, cervix, right and left ovaries, remnants of the right and left fallopian tubes, and the omentum. Dark brown to cream white, nodular to irregular, firm to hard masses replaced approximately 95% of the yellow fibrofatty tissues of the omentum. Several gray, thin-walled cysts measuring 0.5cm - 1cm in greatest dimension were also seen on the surface. Cut sections showed a cream white to tan-red, soft to firm surface with areas of necrosis. The masses were nodular infiltrates even within the yellow, fibrofatty tissues that appeared to be uninvolved on the external surface.

The entire uterus measured 4cm x 3.2cm x 2cm. The cervix was light-tan to cream, with no lesions or areas of hemorrhage. The anterior myometrium measured 1.5cm in thickness, and the posterior myometrium was 1.7cm thick. The outer surface of the uterus showed a tan to dark brown outer surface with several small, cream white to dark brown nodules noted to be adherent to the serosal surface.

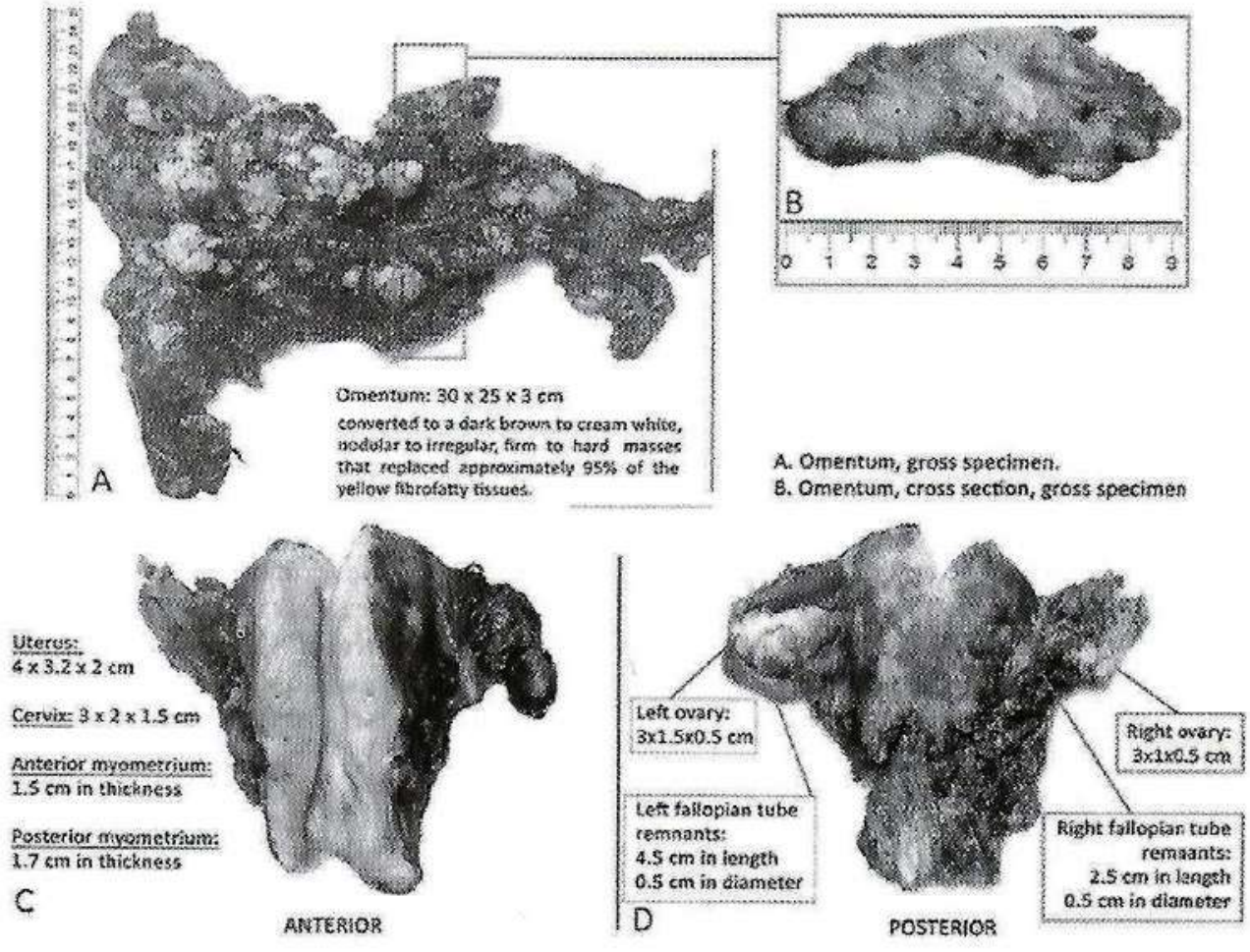


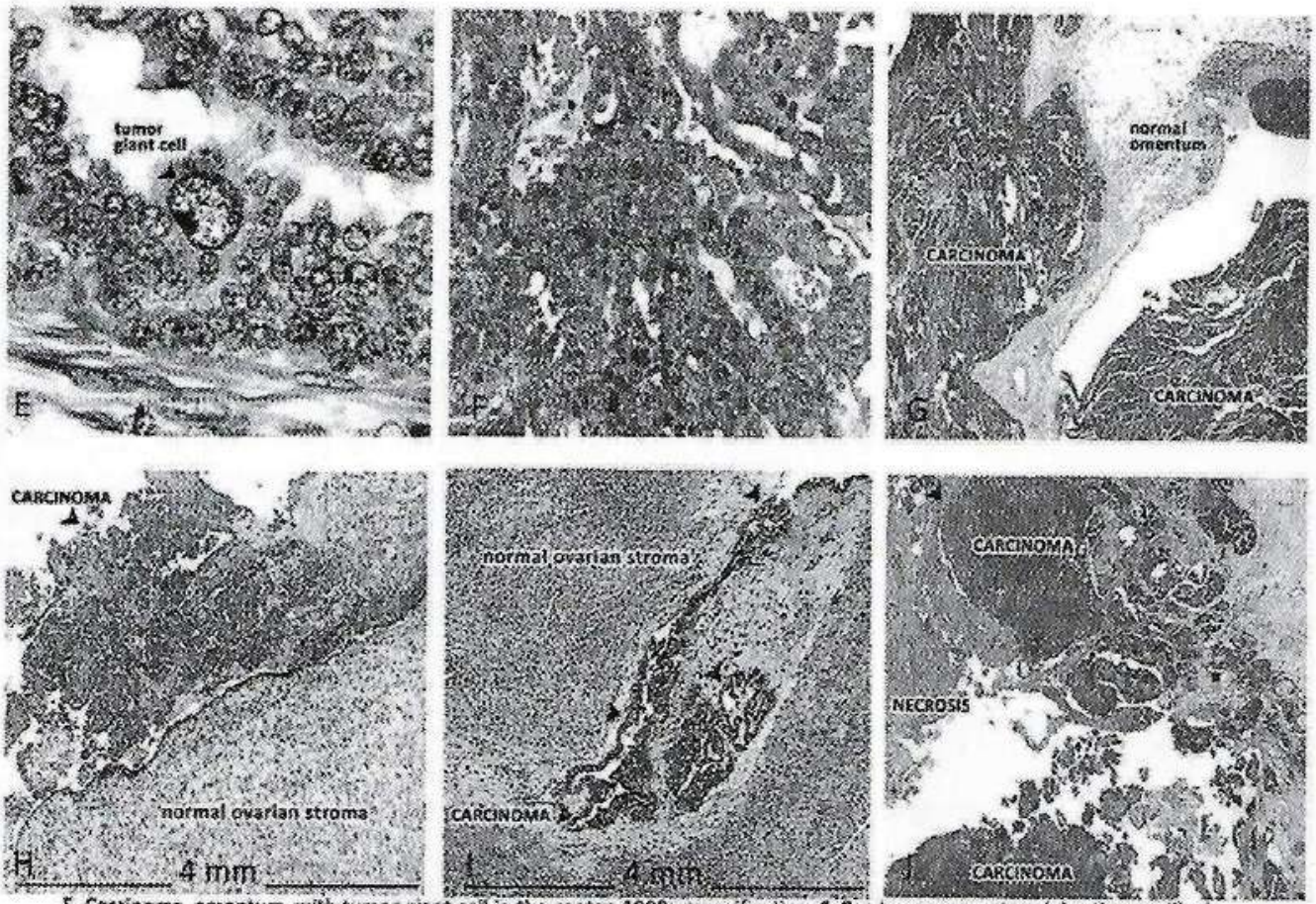
Figure 1. Gross specimen findings of the omentum (A & B), uterus, cervix, right and left fallopian tubes, and right and left ovaries (C & D).

The cut surface of the uterus and cervix showed no evidence of tumor involvement. The right and left ovaries were cream white, firm, and fibrous, and measured 3cm x 1 x 0.5cm and 3cm x 1.5cm x 0.5cm, respectively. Cut sections of both ovaries showed a homogenous, cream white, firm, fibrous surface, with no areas of gross hemorrhage. Several cream white nodules were noted in the outer surface with no gross extension observed within the ovarian stroma. The right and left fallopian tube remnants showed fibromuscular, elongated tissues adherent to the parametrium, and measured 2.5cm long, and 0.5cm in greatest diameter and 0.5cm long and 0.5cm in greatest diameter, respectively. The normal architecture of the right and left fallopian tube remnants could not be clearly delineated with several cream-white to tan brown, nodular to irregular, bosselated tissues adherent to the right and left paratubal tissues. Several nodules were also seen to be adherent to the parametrium.

Microscopic Findings (Figure 2)

Histologic sections of the omentum showed a tumor composed of malignant cells arranged in tubulo-papillary fronds with a fibrovascular core and solid nests with pseudolumen. The cells were ovoid to low cuboidal, with ovoid to pleomorphic large nuclei, coarse to open chromatin pattern, conspicuous to prominent nucleoli, and moderate to scanty basophilic cytoplasm. The lesion was a fungating and infiltrating mass replacing the fibrofatty omental tissues.

The tumor was adherent to the serosal surfaces of the right and left ovaries, remnants of the right and left fallopian tubes, and the parametrial tissues with confluence of the tumor in the lateral thickening of the serosal tissues. The surface of the right and left ovaries exhibited microscopic nodules 3-4 mm in diameter seen on the external surface of the right ovary and encroaching 4 mm into the stroma from



E. Carcinoma, omentum, with tumor giant cell in the center, 1000x magnification. F. Carcinoma, omentum (abortive papillae), 100x magnification. G. Carcinoma with remnants of normal omentum, 40x magnification. H, I. Metastasis to the ovarian serosal surface, right and left ovaries, 40x magnification. J. Metastasis to the paratubal soft tissues, right, 40x magnification.

Figure 2. E-J Microscopic specimen findings of the omentum, parametrium, right and left paratubal serosal surface, and right and left ovarian serosal surface.

the outer surface of the left ovary. Majority of the remaining stroma showed benign tissues with corpora albicantia. The remnants of the right and left fallopian tubes exhibited proliferation of the tumor cells on the paratubal soft tissues, and several islands of tumor cells in the associated lymphatic and vascular channels in the outer portion of the fibromuscular layer. The right and left parametrial tissues showed foci of conglomerations of malignant cells arranged as patchy clusters in the serosa and into the adherent outer muscular layer. Sections from the uterus and cervix did not show any tumor involvement.

Immunohistochemistry Studies (Figure 3)

Immunohistochemistry studies showed diffuse, strong, positive expression for WT1 (nuclear), CA125 (membrane), and EMA (membrane). There was focal expression of ER (nuclear), and CK 5/6 (cytoplasm). There was absent expression of calretinin in the malignant cells; positive expression was noted only in the remnants of the benign mesothelial lining. Ki67 and p53 showed nuclear expression in more than 90% and more than 80% of tumor cells, respectively.

Follow-up and Outcomes

The patient underwent chemotherapy that covered the lesions involving the ovaries, the parametrium, and the omentum. Subsequent serum CA-125 decreased to 5.80 u/mL six months post-operatively, but slowly increased to 5.80, 6.97 and 13.0 u/mL at 10, 11 and 14 months postoperatively, respectively. Since the submission of the surgical specimen for evaluation and definitive diagnosis, there has been no new specimen submitted for histopathologic evaluation that may correspond to a tumor recurrence or metastasis.

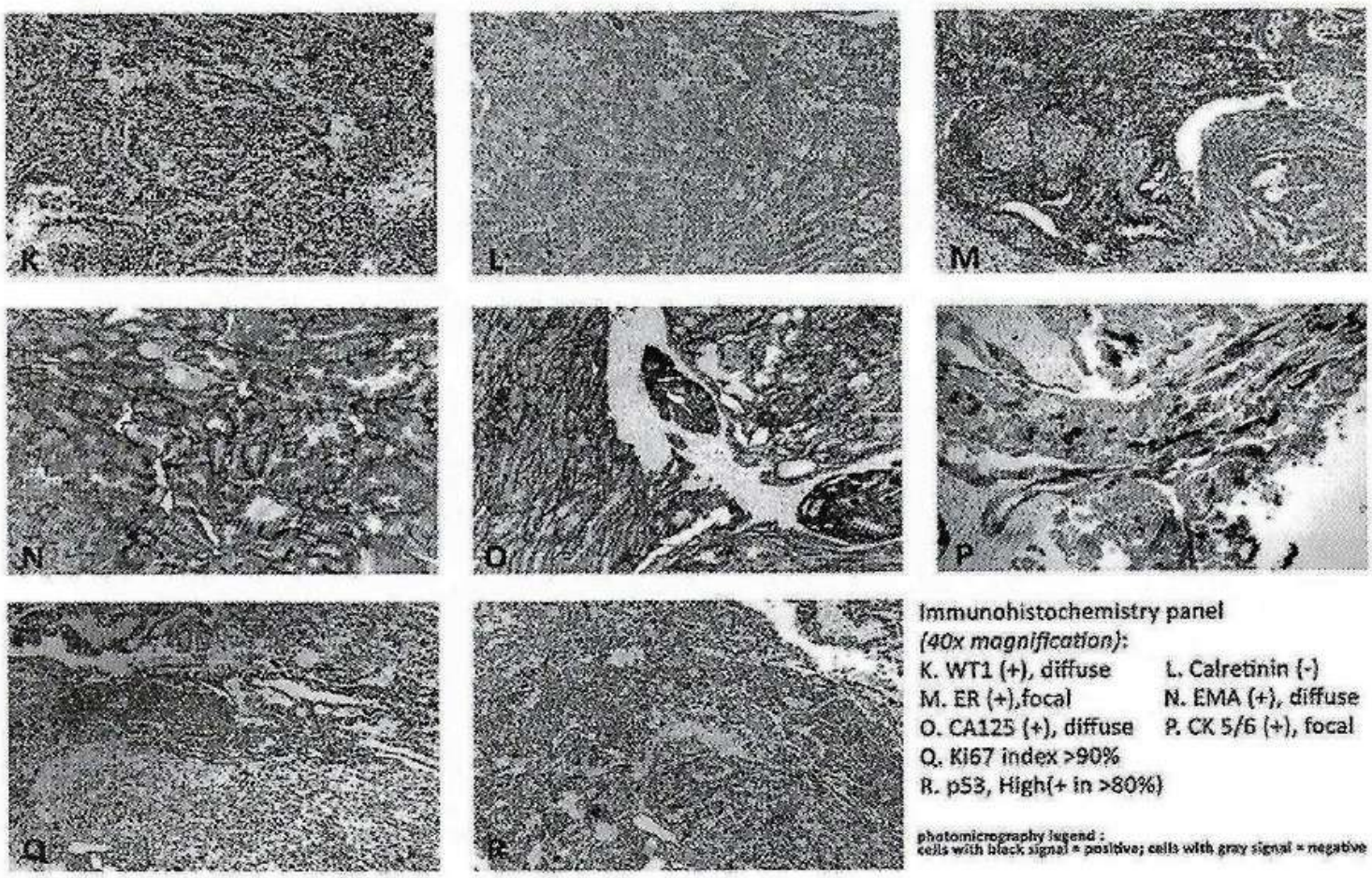


Figure 3. Immunohistochemistry panel findings (K to P)

Discussion

The diagnosis of primary serous papillary carcinoma in this case was established through the step-wise approach of gross and microscopic evaluation with respect to the adaptation of the Gynecologic Oncology Group Guidelines of the College of American Pathology in 2015 for Peritoneal Tumors, and strengthened by the immunohistochemistry profile (Table 1).

In this patient, all the criteria for a primary serous lesion of the peritoneum were fulfilled, with the omentum identified as the site of tumor origin.[3] The immunohistochemistry findings established the difference between the lesion in this case, and malignant mesothelioma, which must be ruled out when evaluating a primary peritoneal lesion. The diagnosis of a serous carcinoma of ovarian primary is also not supported by the immunohistochemistry profile of a focal ER expression in this case, since serous carcinomas from the ovary would more likely have a strong, diffuse positive expression of ER and not a focal expression. The high p53 expression in tumor cells has been used as a surrogate marker for TP53 mutation in high-grade serous carcinoma, as in this case with the p53 expression seen in more than 80% of tumor cells.

Comparison of this case with the twelve published reports discussing the immunohistochemistry profile used after initial morphologic diagnosis and fulfilling the criteria for a primary peritoneal lesion showed that the most commonly utilized stains to characterize the tumor are ER and WT, which are both expressed in this case. Calretinin is consistently negative in serous carcinoma. Although CK 5/6 is commonly negative, focal positive expression of CK 5/6 has been documented in serous carcinoma, as seen in this case, and is differentiated from the diffuse positive expression of CK 5/6 which is seen in malignant mesothelioma (Table 2).[4,5,6-18]

Since the pathogenesis of ovarian serous carcinoma has been greatly studied and the diagnosis of peritoneal serous carcinoma stipulates that it should be similar or identical to those of ovarian serous carcinoma of any grade, it may be postulated that the high-grade serous carcinomas of the peritoneum originate from seeding of tubal epithelium that underwent transformation into a carcinoma, with similar if not identical mutations to those that occur in the ovary, particularly for TP53. Although this should require sequencing of the TP53 of the tumor cells, immunostaining of the p53 has been used as a surrogate marker for TP53 in high-

Table 1. Application of the Gynecologic Oncology Group guidelines

Application of the GOG Criteria for Primary Serous Carcinoma to the Gross and Histologic Findings

Gynecologic Oncology Group (GOG)) Criteria for the Diagnosis of Primary Serous Carcinoma of the Peritoneum Adapted by the Protocol for the Examination of Specimen From Patients with Tumors of the Peritoneum, College of American Pathologists 2015 :	CASE
Both ovaries are either normal in size or enlarged by a benign process	+
The bulk of the tumor involves the peritoneum, or the extent of tumor involvement at 1 or more extraovarian sites is greater than that on the surface of or within either ovary	+
Microscopic examination of the ovaries reveals any of the following:	
(a) no tumor	
(b) tumor confined to the surface epithelium, with no evidence of cortical invasion	
(c) tumor involving the ovarian surface and the underlying cortical stroma, but less than 5 x 5 mm in diameter	+
(d) tumor less than 5 x 5 mm within the ovarian substance, with or without surface involvement	
The histologic and cytologic characteristics of the tumor are predominantly serous and similar or identical to those of ovarian serous papillary carcinoma of any grade.	+
If an oophorectomy has been performed in the past, a confident diagnosis of primary peritoneal serous carcinoma requires 1 of the following: (a) a pathology report to document the absence of carcinoma in the ovarian specimen, with review of all the slides if the oophorectomy has been performed within 5 years of the current procedure (b) if the oophorectomy has been performed more than 5 years before the current procedure, the pathology report of the specimen should be obtained, and the slides should be reviewed if still available. The peritoneal tumor should be interpreted in light of the ovarian findings.	NO HISTORY OF PRIOR OOPHORECTOMY

Table 2. Comparison of the Immunohistochemistry Panel findings.

Comparison of IHC Characteristics of Ovarian and Peritoneal Serous Carcinomas with the Case

IHC	Immunoreactivity Patterns of Serous Carcinoma (Adapted from S Nofech-Mozes et al. 2008 [14]		IHC PATTERN OF THE CASE
	Ovary	Peritoneum	
WT1	Strong, diffuse	Strong, diffuse to weak, focal	Strong, diffuse
P53	More commonly Strong, diffuse	Strong, diffuse	Strong, diffuse
ER	More commonly strong, diffuse	More commonly weak, focal to moderate, focal; may be absent	Moderate, focal
CK 5/6	More commonly absent	More commonly absent	Moderate, focal

Comparison of IHC Characteristics of Malignant Mesothelioma and Serous Carcinomas with the Case

IHC	Immunoreactivity Patterns of Malignant Mesothelioma Vs High Grade Serous Carcinoma (Ordoñez 2006)		IHC PATTERN OF THE CASE
	Malignant Mesothelioma	High Grade Serous Carcinoma	
Calretinin	Strong, diffuse	Absent	Absent
CK 5/6	Strong, diffuse	Moderate, focal	Moderate, focal
CA-125	Strong, diffuse	Strong, diffuse	Strong, diffuse
EMA	Strong, diffuse	Strong, diffuse	Strong, diffuse

grade serous ovarian carcinoma and may be applied to the peritoneal counterpart as well.[14,19]

The diagnosis of primary serous papillary carcinoma was established through the stepwise approach of gross and microscopic evaluation with respect to the adoption of the Gynecologic Oncology Group Guidelines of the College of American Pathology in 2015 for Peritoneal Tumors, and strengthened by the immunohistochemistry profile. This report contributes to the fund of knowledge of the clinical presentation, morphologic findings, and immunohistochemistry profile pertinent to this rare lesion for better understanding, leading to prompt diagnosis and improved quality of care.

Informed Consent

The authors did not perform any procedure on the patient. This case report included only the specimen submitted by the attending physician to the Section of Anatomic Pathology for surgical histopathology evaluation with full, informed consent for specimen evaluation and academic discussion.

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The role of bariatric and metabolic surgery on mildly obese diabetic patients

Katherine G. Ordinario, MD and Emmanuel S. Astudillo, MD

Abstract

Introduction Bariatric surgery has been incorporated in the care of diabetic patients with a body mass index greater than 35 kg/m^2, however a segment of the diabetic population has a body mass index 30 to <35 kg/m2. This meta-analysis aimed to determine the effects of bariatric surgery in mildly obese diabetic patients in terms of remission of the disease, change in HbA1c and fasting blood sugar levels.

Methods Randomized controlled trials on adult patients with type 2 diabetes with body mass index < 35 kg/m^2 that compared bariatric surgery with non-surgical management were considered in this study. The primary outcomes of interest were remission of diabetes mellitus, changes in body mass index, glycosylated hemoglobin and fasting blood sugar levels and in weight. The odds ratio was the primary measure of treatment effect; 95% confidence intervals were utilized. Heterogeneity were assessed by Q-square (v^2) and I-square statistics (I^2). Meta-analysis with forest plot was performed using Review Manager Version 5.3.

Results Remission of diabetes was achieved in 69 out of 94 patients (73%) in four studies included in the analysis (OR = 79.07, 95% CI 12.36, 506.3). Decrease in glycosylated hemoglobin, fasting blood sugar, body mass index, weight, total cholesterol, triglycerides and increase in HDL was greater in the surgical arms of all the included studies.

Conclusion Bariatric surgery is a rapid, effective and sustainable treatment option for the resolution of type 2 diabetes mellitus even among mildly obese patients. It is effective in improving or resolving diabetes- and obesity-related diseases such as dyslipidemia.

Key words: Bariatric surgery, metabolic surgery, diabetes mellitus, obesity

Type 2 diabetes mellitus (T2DM) is a disease that affects people worldwide across all social classes and races. Diabetes is a major cause of blindness, kidney failure, heart attack, stroke and lower limb amputation. The number of people with diabetes had risen to 422 million in 2014 from 108 million in 1980.[1] By 2025, it is predicted that more than 330 million people will have acquired the disease.[1]

Bariatric surgery has now become a standard of care for patients with body mass index (BMI) of 40 kg/m^2 or higher, or for patients with BMI greater than 35 kg/m^2 with obesity-related comorbidities, or obese patients who failed lifestyle and medical management.[2] However, many diabetics belong to the mildly obese population whose BMI ranges from 30 to < 35 kg/m^2.[3] At present, few studies have investigated the effects of bariatric surgery on this population. This meta-analysis aimed to determine the effects of bariatric surgery in type 2 diabetic patients with BMI <35 kg/m^2. This study specifically

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looked into the effect of bariatric surgery on remission of diabetes, HbA1c and fasting blood sugar levels. The other outcomes of interest were change in BMI, body weight, and blood lipids.

Methods

Randomized controlled trials on adult patients with type 2 diabetes with BMI < 35 kg/m^2 that compared bariatric surgery with non-surgical management were considered in this study. Bariatric surgery was not limited to any specific type or technique. The study should have one or more of the following outcomes: remission of diabetes, change in HbA1c and/or fasting blood sugar, change in BMI and/or weight and change in serum lipids. Review articles, retrospective analyses, observational studies, and abstracts were not considered

An electronic search of the databases EBSCOHost, PubMed, ClinicalKeys, and Cochrane using the following keywords: "bariatric surgery", "metabolic surgery", "BMI", "BMI less than 35 kg/m^2", "BMI < 35 kg/m^2", "diabetes mellitus type 2", "T2DM" was made. A comprehensive search of reference lists of published articles and review articles was performed to ensure inclusion of all possible studies and exclusion of duplicates. The authors included articles in English, whose full text was available, and published up to the end of March 2017.

All potential trials were selected for eligibility according to the criteria specified in the research protocol. Two reviewers (ESA and KGO) extracted data from each publication. The quality of included studies was assessed independently by the two reviewers using the Cochrane Handbook for Systematic Reviews of Interventions. The following parameters were assessed: random sequence generation, allocation concealment, blinding of the patient and the observer, blinding of the outcome assessment, incomplete outcome data, and selective outcome reporting.

The odds ratio (OR) was used as the primary measure of treatment effect; 95% confidence intervals (CI) for OR were utilized. Heterogeneity were assessed by Q-square (v^2) and I-square statistics (I^2). An I^2 value greater than 50% was considered as substantial heterogeneity. Meta-analysis using a fixed-effects model and generation of Forest plot was performed using Review Manager Version 5.3.

Results

Four RCTs were included in the meta-analyses and their characteristics are summarized in Table 1.[5-8] The four studies included a total of 263 adult patients with a mean age of 49 years, mean BMI of 31.2 kg/m^2, mean HbA1c of 8.8%, and mean weight of 87.7 kg. One hundred thirty-seven patients were randomized to bariatric surgery and 126 to nonsurgical regimens and followed up for 6 to 36 months. The four studies used different techniques of bariatric surgery such as laparoscopic Roux en Y gastric bypass, laparoscopic gastric banding or laparoscopic sleeve gastrectomy. The non-surgical regimens included usual care with or without

Table 1. Characteristics of included studies

Study	Population	Bariatric surgery	Nonsurgical management	Follow up
Liang, 2013	108 patients, 30-60 y/o, BMI > 28 kg/m^2	Laparoscopic Roux-en-Y gastric bypass (59)	Usual care (15), usual care + exenatide (34)	1 year
Parikh, 2014	57 patients, BMI 30-35 kg/m^2	Laparoscopic Roux-en-Y gastric bypass or laparoscopic gastric binding or laparoscopic sleeve gastrectomy (33)	Intensive medical weight management (24)	6 months
Scopinario, 2104	47 patients, 35-70 y/o, BMI 30.0-34.9 kg/m^2	Laparoscopic Roux-en-Y gastric bypass (20)	Usual care (27)	36 months
Wentworth, 2014	51 patients, 18-65 y/o, BMI 25-30 kg/m^2	Laparoscopic adjustable gastric banding (25)	Multidisciplinary diabetic care (26)	2 years

exenatide, intensive medical weight management, and a multidisciplinary approach. The risk of bias was low in terms of all parameters except for blinding, as seen in Figure 1.

Remission of T2DM was achieved in 69 out of 94 patients (73%) in the surgical arms of all studies included in the analysis compared with two patients in the nonsurgical groups. The fixed-effects model favored bariatric surgery but showed significant heterogeneity. The random effects model favored bariatric surgery (OR = 79.07, 95% CI 12.36, 506.3); heterogeneity was still significant at 52%, as seen in Figure 2.

The baseline mean HbA1c was 8.6% in the surgical arm and 9.1% in the non-surgical arm. These decreased to 6.3% and 7.5%, respectively, post intervention. Greater decreases in HbA1c were noted on the surgical interventions in all the studies included. The mean difference of 1.11% was significant ($p < 0.001$, 95% CI 0.86, 1.35). Heterogeneity was significant (Figure 3).

The baseline mean FBS were 13.2 and 14.1 mg/dL for surgical and non-surgical arms, respectively, and decreased to 12.1 and 11.3 mg/dL, respectively. The mean decrease was 19.09% and was significant ($p < 0.001$, 95% CI 14.00, 24.18). Heterogeneity was significant (Figure 4).

The baseline BMI for the surgical and non-surgical arms were 31.2 and 31.1 kg/m^2, respectively, and decreased to 25 and 29.8 kg/m^2, respectively. The mean decrease was 3.96% and was significant ($p < 0.001$, 95% CI 3.86, 4.05). Heterogeneity was significant (Figure 5).

Weight loss was measured and achieved in the all the arms of the three studies included in this analysis. The baseline mean weights for surgical and non-surgical arms were 86.3 and 87.2 kg and decreased to 68.9 and 85.6 kg, respectively. The decrease in weight was greater in the surgical arms with a mean difference of 22.8% ($p < 0.001$, 95% 22.18, 23.38). Heterogeneity was significant (Figure 6). Percent excess weight loss (%EWL), a common metric for reporting weight loss after bariatric surgery was measured in only one of the studies. Parikh reported the %EWL for bariatric surgery at 60% compared to the non-surgical arm (7.4%).[7]

The mean baseline cholesterol levels for both surgical and non-surgical arms was 5 mmol/L and decreased to 3.7 and 4.3 mmol/L, respectively, after the interventions. There was a greater decrease in levels in the medical arms of most studies. The overall results still favored bariatric surgery (Figure 7).[5] The initial mean HDLs for surgical and non-surgical arms were 1.08 and 1.04 mmol/L and increased to 1.31 and 1.05 mmol/L, respectively, post interventions. HDL had a greater increase in the surgical arms in the studies included except for Parikh. Overall results favored bariatric surgery (Figure 8). There were greater decreases in LDL and triglycerides in the surgical arms as seen in Figures 9 and 10.

Discussion

Humanity has been looking for ways to treat type 2 diabetes mellitus for centuries, or minimize or delay the onset of complications. The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014. In 2012,

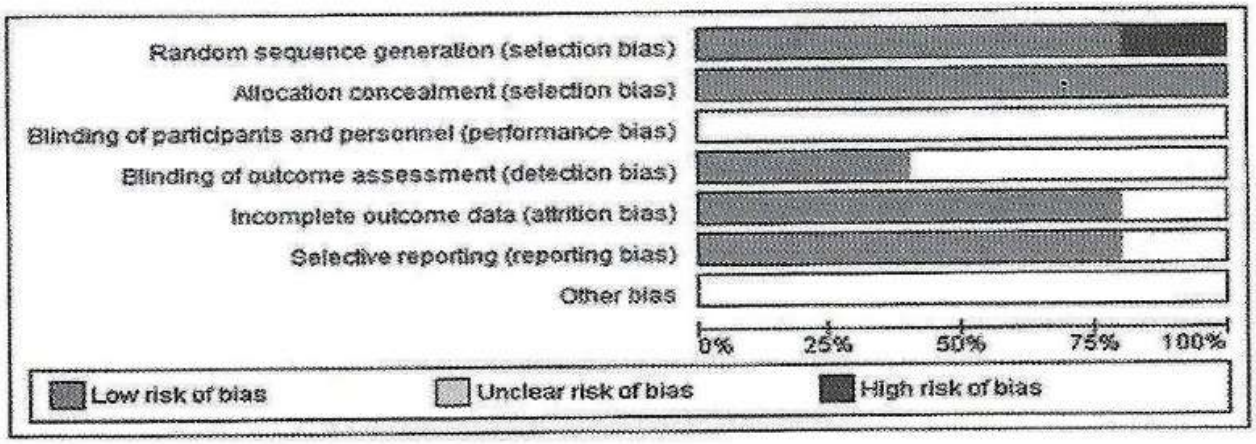

Figure 1. Risk of bias graph

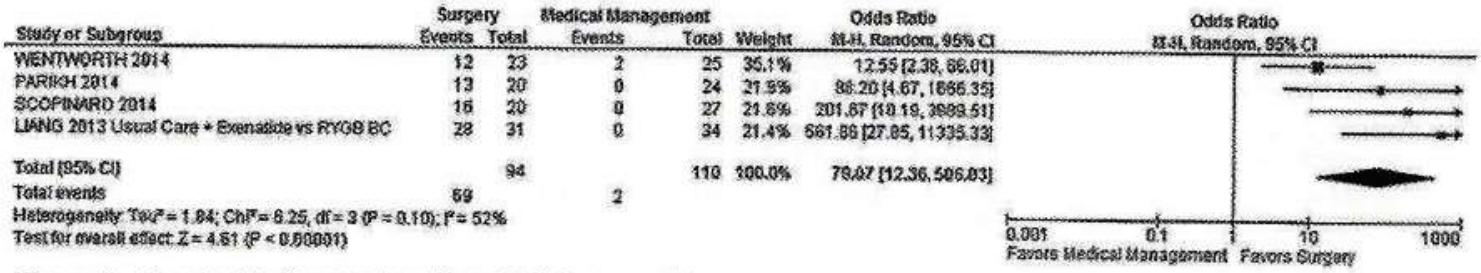

Figure 2. Forest plot of remission of type 2 diabetes mellitus.

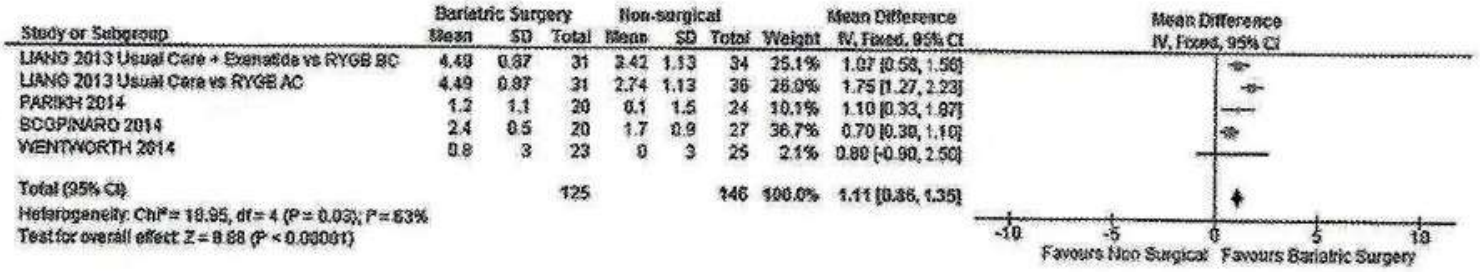

Figure 3. Forest plot of mean change in HbA1c.

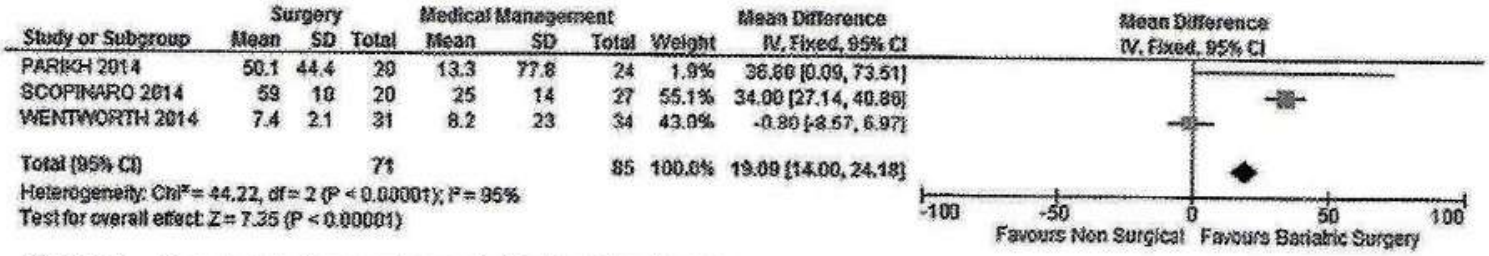

Figure 4. Forest plot of mean change in fasting blood sugar.

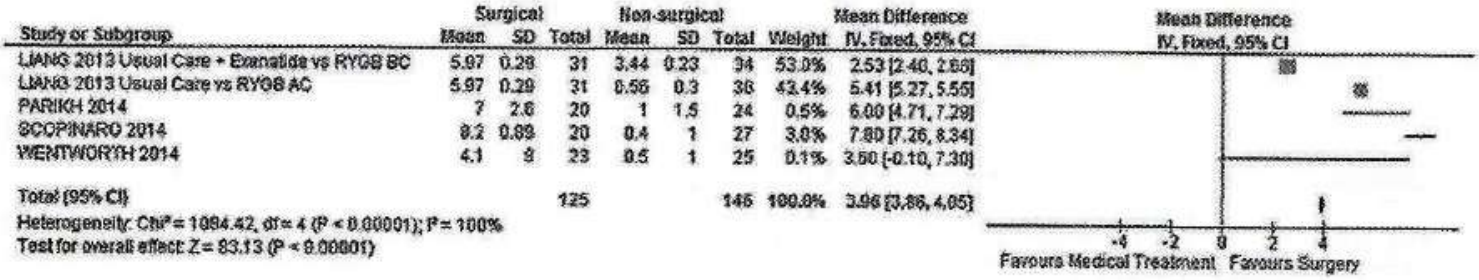

Figure 5. Forest plot of mean change in BMI.

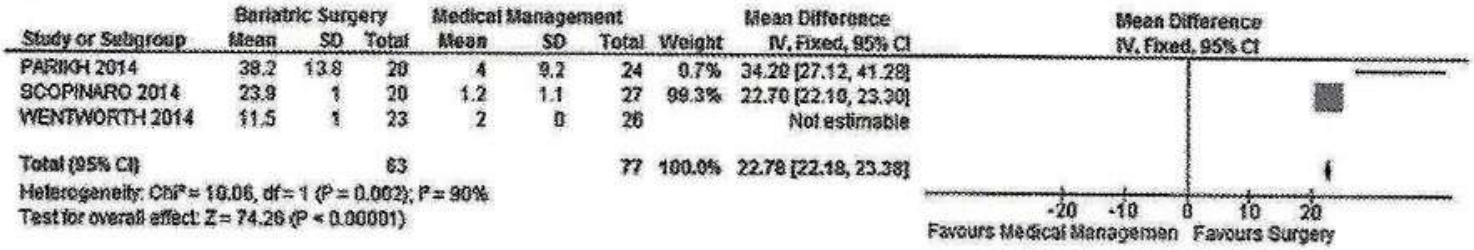

Figure 6. Forest plot of mean change in weight.

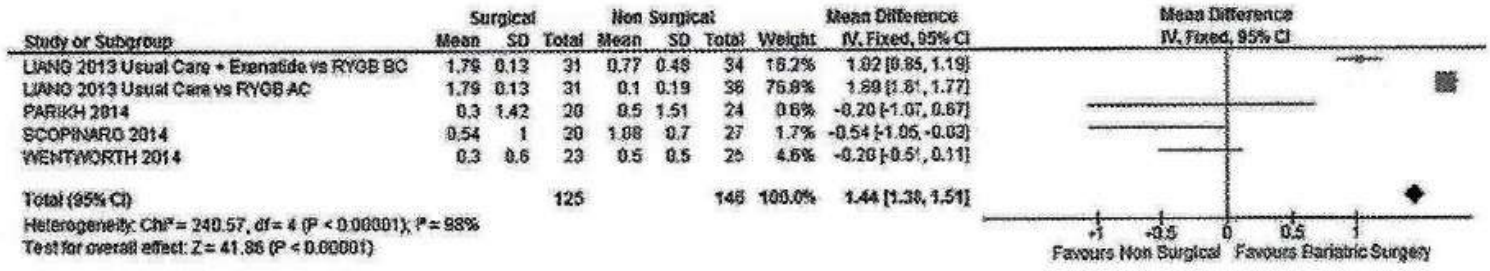

Figure 7. Forest plot of mean change in total cholesterol.

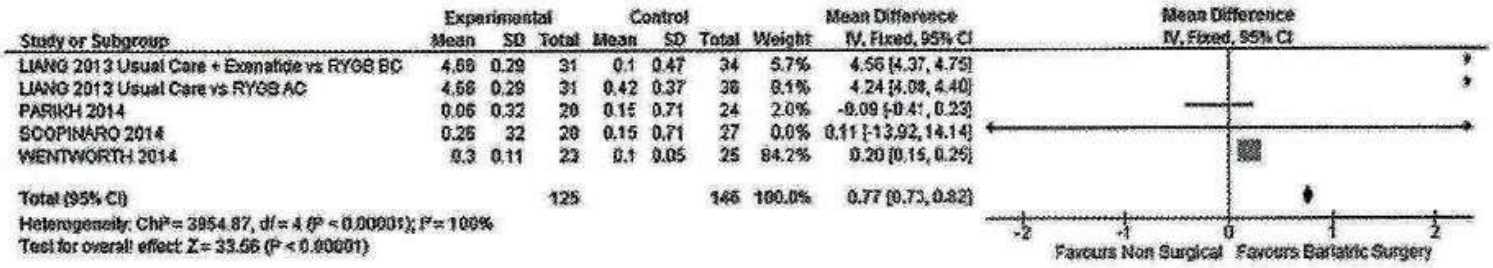

Figure 8. Forest plot of mean change in HDL.

Figure 9. Forest plot of mean change in LDL.

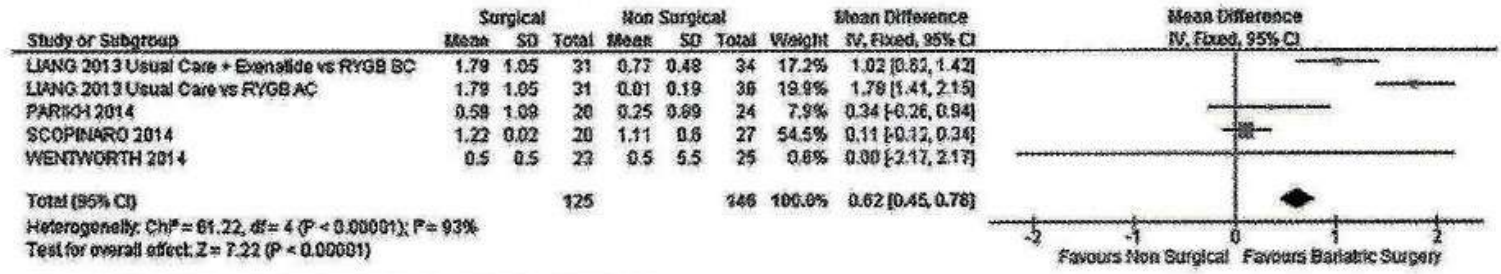

Figure 10. Forest plot of mean change in triglycerides.

an estimated 1.5 million deaths were directly caused by diabetes; 2.2 million deaths recorded that year were attributable to high blood glucose, half of which occurred prematurely, before age 70. It is projected that diabetes will be the seventh leading cause of death in 2030. This compels us to look for a treatment that will help control this epidemic of diabetes.

Bariatric surgery was initially developed as a treatment option for obesity. It now presents itself in this age as an option for the treatment of diabetes mellitus. It has now become a standard of care for patients with BMI of 40 kg/m^2 or higher, or BMI greater than 35 kg/m^2 with obesity related comorbidities, or obese patients who fail lifestyle and medical management.[9] There are different techniques of bariatric surgery, the gold standard of which is the Roux-en-Y gastric bypass (RYGB). Bariatric surgeries all commonly reduce gastric volume which reduces food intake. Reduction in intestinal mucosal area leads to lesser nutrient absorption and lesser caloric intake. Gastric volume restriction also leads to early satiety. This leads to improvement of hepatic insulin sensitivity and improves insulin clearance in the liver. Additionally, caloric restriction reduces hyperinsulinemia and provides "rest" for the beta-cell, which results in enhanced beta-cell function. This in turn decreases the deposition of lipid metabolites in adipose and extraadipose tissue, such as skeletal muscles and liver and corrects the impaired adipose tissue signaling.[9] Insulin sensitivity is also accompanied by elevated adiponectin (a cytokine released by adipose tissue that decreases insulin resistance) levels, enhanced insulin-receptor concentration and markers of insulin signaling in key target tissues. This will lead to the lowering of fasting glucose levels.[9,10] Aside from these mechanical effects of bariatric surgery, it has been found that gut hormones such as glucagon-like peptide-1 (GLP1), peptide YY (PYY) and ghrelin contribute to maintain weight loss and changes in glucose homeostasis.[11] Recently, changes in gut microbiota were thought to be involved in obesity. Obese mice that underwent RYGB surgery had sustained increase in the relative abundance of Escherichia and Akkermansia in the gut microbiome and expected weight loss whereas mice that underwent the sham surgery did not. These changes were noted to be independent of weight change and caloric restriction, and were detectable throughout the length of the gastrointestinal tract and were most evident in the distal gut, downstream of the surgical manipulation site. Transfer of the gut microbiota from RYGB-treated mice to non-operated, germ-free mice resulted in weight loss and decreased fat mass in the recipient animals. These findings may prove that changes in gut microbiota contribute to reduced host weight and adiposity after RYGB surgery.[12]

Bariatric surgery is now recommended for patients with BMI of 40 kg/m^2 or higher, or for patients with BMI greater than 35 kg/m^2 with obesity related comorbidities, or obese patients who failed lifestyle and medical management, as mentioned earlier.[2] However, for many diabetic patients whose BMI are < 35kg/m^2, there is no recommendation yet. The resolution of the diabetes mellitus in all the studies investigated proves that bariatric surgery is able to achieve remission from the disease. In the study of Parikh, in as early as six months from the time of operation, remission was observed among 13 out of 20 patients who underwent surgery compared to no subjects achieving remission in the intensive medical weight management, pharmacotherapy and non-surgical weight loss groups.[7] In the study of Wentworth, which measured remission from diabetes mellitus for a span of two years, 12 out of 23 (52%) patients who underwent gastric banding versus 2 out of 25 (8%) in the multidisciplinary care group achieved remission.[6]

It has been established that bariatric surgery reduces weight. Obesity (BMI ≥ 25 kg/m^2) is a known risk factor of diabetes mellitus and they usually occur together.[5] Body weight loss is known to be effective in improving T2DM and is part of the conventional treatment plan. However successful long-term treatment of obese T2DM requires maintenance of achieved weight which is hard. Hence, bariatric surgery is considered in the treatment plan. In the study of Parikh, the patients who underwent surgery lost more weight (7.0 BMI decrease vs. 1.0 BMI decrease, $p < 0.001$). In the study of Wentworth, weight loss was the most strongly associated factor with diabetes remission.[6]

Hemoglobin A1c is the standard method for assessing long-term glycemic control. This is a reflection of the glycemic control over the previous 2 to 3 months as well as the primary predictor of long-term complications of diabetes.[13] Fasting blood sugar is used to diagnose type 2 diabetes mellitus. High blood glucose levels are a major source of mortality and morbidity.[1] In the studies investigated, it was noted that there were greater decreases in FBS in the bariatric arms than in the non-surgical arms. According to Wentworth, low baseline fasting

glucose and HbA1c were associated with diabetes remission.[6] Poor glucose control has been associated with reduced likelihood of diabetes remission after bariatric surgery.[6]

The surgery group compared to medical weight management arm in the study of Parikh had lower HbA1c (6.2 vs. 7.8%, p = 0.002), lower fasting glucose (99.5 vs. 157mg/dL, p = 0.0068) and fewer T2DM medication requirements (20% vs. 88%, p < 0.001) at 6 months post intervention.[7]

Several studies have shown that bariatric surgery has been found to be significantly more efficient than medical treatment alone, with regard to control of dyslipidemia.[14,15] In this meta-analysis, HDL levels were noted to decrease after surgery and surgery plus exenatide in the study of Liang.[5] In the study of Wentworth, only triglycerides were noted to have shown significant decrease after two years.[6] In the study of Scopinaro, triglyceride showed reduction during the first year of the study and was noted up to the third year. Similarly, there was also a significant decrease of mean serum total cholesterol from 55 to 20 %.[8] HDL cholesterol also progressively increased from 38 to around 50 mg/dL. Normal levels were achieved by the fourth postoperative month.[8] Bariatric surgery corrects impaired lipid processing of the body by inducing weight loss and improving insulin-dependent glucose uptake. It may also be brought about by changes in neuroendocrine hormones, such as GLP1, PYY, and ghrelin.[9]

The length of follow up was different across the four studies. The shortest duration of follow up was six months and the longest was two years. This proves that remission of diabetes mellitus can be observed even after at least two years from operation. However, others have shown decrease in blood sugar one day after surgery and remission lasting up to fifteen years.

Bariatric surgery is an innovation that was initially intended for the treatment of morbid obesity but is now being utilized as a standard of care in the management of type 2 diabetes. This gives hope to diabetic patients who are mildy obese. This meta-analysis shows that bariatric surgery is a rapid, effective and sustainable treatment option for the resolution of type 2 diabetes mellitus even among mildly obese patients. It is effective in improving or resolving diabetes- and obesity-related diseases such as dyslipidemia.

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Instructions to Authors

Aim and Scope

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All contributions should be written in English. Papers should be written to be intelligible to the professional reader who is not a specialist in the field. The editor and his staff reserve the right to modify manuscripts to eliminate ambiguity and repetitions, and to improve communication between author and reader. If extensive alterations are required, the manuscripts will be returned to the author for revision. Therefore, to minimize delay in publication, manuscripts should be submitted in accordance with the instructions detailed herein. The author may refer to the *Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals 2017* available at www.icmje.org for additional guidance. The editor will not be held responsible for views expressed in this journal.

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A copy of the manuscript, including tables and figures, should be submitted to the editor. The manuscript should be typed on short bond paper, in a single column, double-spaced all throughout, using Times New Roman or Arial 12. Tables, figures and illustrations should be in separate sheets (not embedded in the text). This should be accompanied by a cover letter containing the following: 1) corresponding author with complete contact details; 2) signed declaration by all authors of their involvement and willingness to take public responsibility for the paper's contents; 3) ethics approval when applicable; 4) declaration that the paper has not been published and is not under consideration for publication in another journal; 5) declaration of support/funding when applicable; and 6) declaration of conflict of interest. To facilitate revision of the manuscript, the editor requires submission of an electronic copy in Microsoft Word.

All pages of the typed manuscript should be numbered, including those containing acknowledgments, references, tables, and figures. The manuscript should be arranged as follows: 1) title and list of authors, 2) corresponding author with contact details, 3) abstract, 4) key words, 5) introduction, 6) methods, 7) results, 8) discussion, 9) acknowledgments, 10) support/funding, 11) conflict of interest declaration, 12) references, 13) tables, and 14) figures and figure legends.

Title, list of authors, corresponding author

The title should be as concise and informative as possible and should contain all key words to facilitate indexing and information retrieval. This should be followed by the list of authors' names to be written as follows: first name, middle initial, family name and highest academic degree. The sequence of names should be agreed upon by the authors. The department or institution of each of the authors should also be provided. Only those qualified based on the *Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals 2017* should be listed as authors. The contact details (affiliation, address, email address, contact number) of the corresponding author should be provided.

Abstract

This should be a concise structured summary consisting of the Introduction, Methods,

Results and Conclusion. It should be no more than 200 words and include the purpose, basic procedures, main findings and principal conclusions of the investigation. New and important information should be emphasized.

Key Words

Two to six key words or phrases, preferably MESH terms, should be provided. This will assist in cross-indexing the article.

Introduction

This should contain a summary of the rationale and objectives of the study and provide an outline of pertinent background material. It should not contain either results or conclusions.

Methods

This should adequately describe the study design, population, selection process, randomization, blinding, study procedures, data collected and statistical methods used in data analysis.

Results

This should be presented in logical sequence in the text, tables, and figures avoiding repetitive presentation of the same data. Measurements should be in International System (SI) units. This section should not include material appropriately belonging to the discussion. Results must be statistically analyzed when appropriate.

Discussion

Data mentioned in the results should be explained in relation to any hypothesis advanced in the introduction. This may also include an evaluation of the methodology and the relationship of new information to previously gathered data. Conclusions should be incorporated in the final paragraph and should be commensurate with and completely supported by data gathered in the study.

Acknowledgments

Only persons who have made genuine contributions and who endorse the data and conclusions should be acknowledged. Authors are responsible for obtaining written permission to utilize any copyrighted text and/or illustrations.

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Francis D, Hadler SC, Thompson S, et al. The prevention of hepatitis B with vaccine: Report of the Centers for Disease Control multi-center efficacy trial among homosexual men. Ann Intern Med 1982; 97: 362-6.

Krugman S, Overby LR, Mushahwar IK, et al. Viral hepatitis type B: studies on the natural history and prevention reexamined. N Engl J Med 1979; 300: 101-6.

Nyland LJ, Grimmer KA. Is undergraduate physiotherapy study a risk factor for low back pain? A prevalence study of LBP in physiotherapy students. Retrieved from: http://www.Biomed-central.com/1471-2474/4/22. 2003. [Accessed August 27, 2011].

Rankin J, Tennant PW, Stothard KJ, et al. Maternal body mass index and congenital anomaly risk: A cohort study. Int J Obes 2010; 34(9): 1371-80. Available from: http://ncbi.nlm.nih.gov/pubmed/20368710. [Accessed August 27, 2011].

Books and other monographs

Personal authors

Adams RD, Victor M. Principles of Neurology. New York: McGraw-Hill; 1981.

Chapter in a book

Corbett S. Systemic Response to Injury and Metabolic Support. In: Brunicardi FC (editor). Schwartz's Principles of Surgery. 10th ed. New York: McGraw-Hill; 2015: 13-50.

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