

行政院國家科學委員會補助 專題研究計畫成果報告

同時多發性肺癌的臨床病理與免疫組織化學研究及
其與病人預後之相關

The clinicopathological and immunohistochemical studies of synchronous
multifocal non-small cell lung cancer-its prognostic significance

計畫類別： ☒ 個別型計畫 ☐ 整合型計畫

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本成果報告包括以下應繳交之附件：

- ☐ 赴國外出差或研習心得報告一份
- ☐ 赴大陸地區出差或研習心得報告一份
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- ☐ 國際合作研究計畫國外研究報告書一份

執行單位：台大醫學院外科

中 華 民 國 91 年 01 月 09 日

A Clinicopathological Study of Synchronous Multifocal Non-Small Cell Lung Cancer

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Synchronous multifocal involvement in non-small lung cancer (NSCLC) was not an unusual occurrence, especially in histological types of adenocarcinoma and bronchioloalveolar carcinoma. The TNM staging and prognosis in these tumors are still remained as an unsolved problem. During the period from Jan 1990 to Apr 1998, 50 patients were pathologically proved to have multifocal tumors after surgically resection. The incidence was 9% among the surgically resected NSCLC patients done in the same period. There were 30 males and 20 females, with age ranging from 46 to 80 years. The distribution of histological type was adenocarcinoma in 29 patients, bronchioloalveolar carcinoma in 17, squamous cell carcinoma in 2 and adenosquamous carcinoma in 2. The tumors were located within one lobe in 30 patients and more than one lobe in 20 patients, including 2 had contralateral tumor. An immunohistochemical studies of P53, Rb, E-cadherin, PCNA and Ki67 expressions in these tumors were conducted. And their relations to clinical and pathological characteristics were analysed. The analysis of patient's survival revealed significant worse factors including positive regional lymph node involvement, pathological evidence of vascular invasion, and positive P53, PCNA or Ki67 expression.

Synchronous Multiple NSCLC

- Intrapulmonary metastasis ?
- Multiple primary lung cancers ?

Remained as a difficult problem in TNM staging of the tumor

1996 AJCC and UICC

- NSCLC with satellite nodule(s) with ipsilateral primary-tumor lobe — T4
- Separate tumor nodule(s) in the ipsilateral non-primary-tumor lobe — M1

Synchronous Multiple NSCLC

- Incidence
- Pathological characteristics
- Prognosis

Patients and Methods

Period: Jan 1990 to Apr 1998

No. of patients: 50 patients with pathologically proved
to have multifocal tumors

Male: 30 **Female:** 20

Age: 46 – 80 years

Pathological Studies

- **Histological type, local invasion, regional lymph node involvement, vascular invasion**
- **Immunohistochemistry:**
P53, Rb, E-cadherin, PCNA, Ki-67

Distribution of Histological Type

- Adenocarcinoma : 29
- Bronchioloalveolar Ca : 17
- Squamous cell Ca : 2
- Adenosquamous cell Ca : 2

Location of Multifocal Tumors :

- Within one lobe : 30 patients
- ≥ two lobes : 20 patients
(contralateral : 2)
- No. of tumors :
- 2 : 9 patients
 - > 2 : 41 patients

All 50 patients had undergone complete surgical resection

Pneumonectomy : 7 Lobectomy + wedge : 7
Bilobectomy : 5 Segmentectomy + wedge : 1
Lobectomy : 29 Segmentectomy : 1
Operative mortality : 1 (2.0%)

Within one lobe :

40% have clinical symptoms

3.3% have recurrent tumor after operation

≥ two lobes :

80% have clinical symptoms

25% have recurrent tumor after operation

Results of Immunohistochemical Study

Significant correlation :

P53 : Ki67, PCNA, LN metastasis, survival

Rb : P53 (inverse)

E-cad : vascular invasion

Ki67 : P53, PCNA, tumor size, survival

PCNA : P53, Ki67, vascular invasion, survival

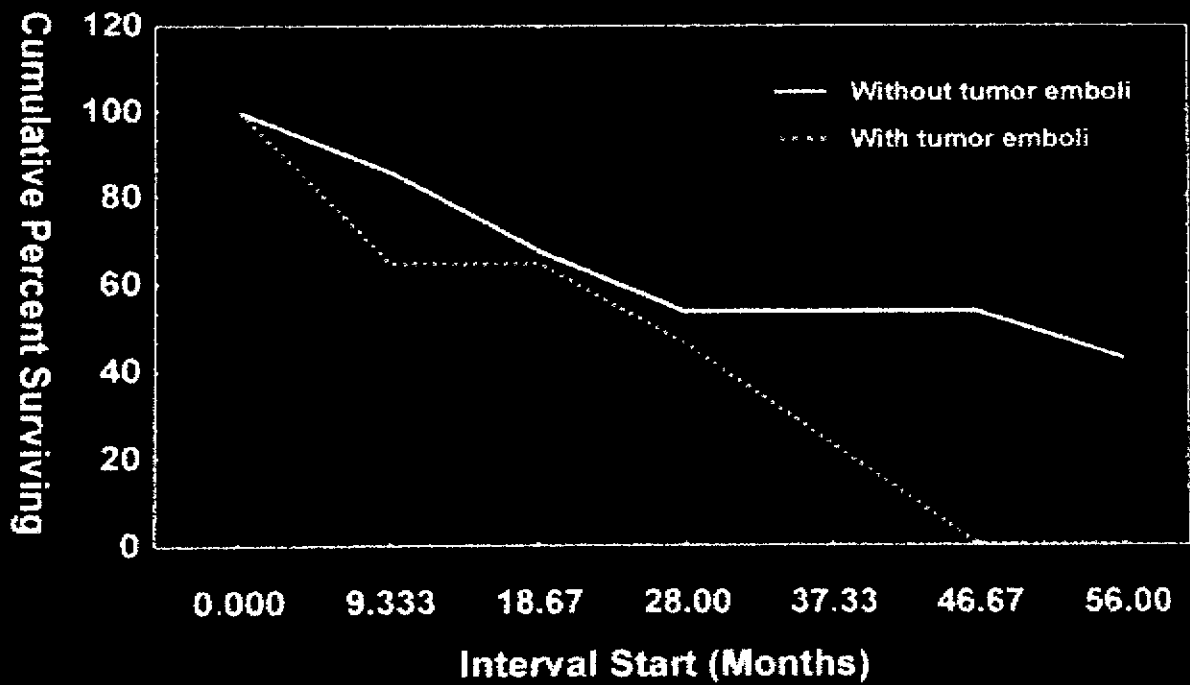
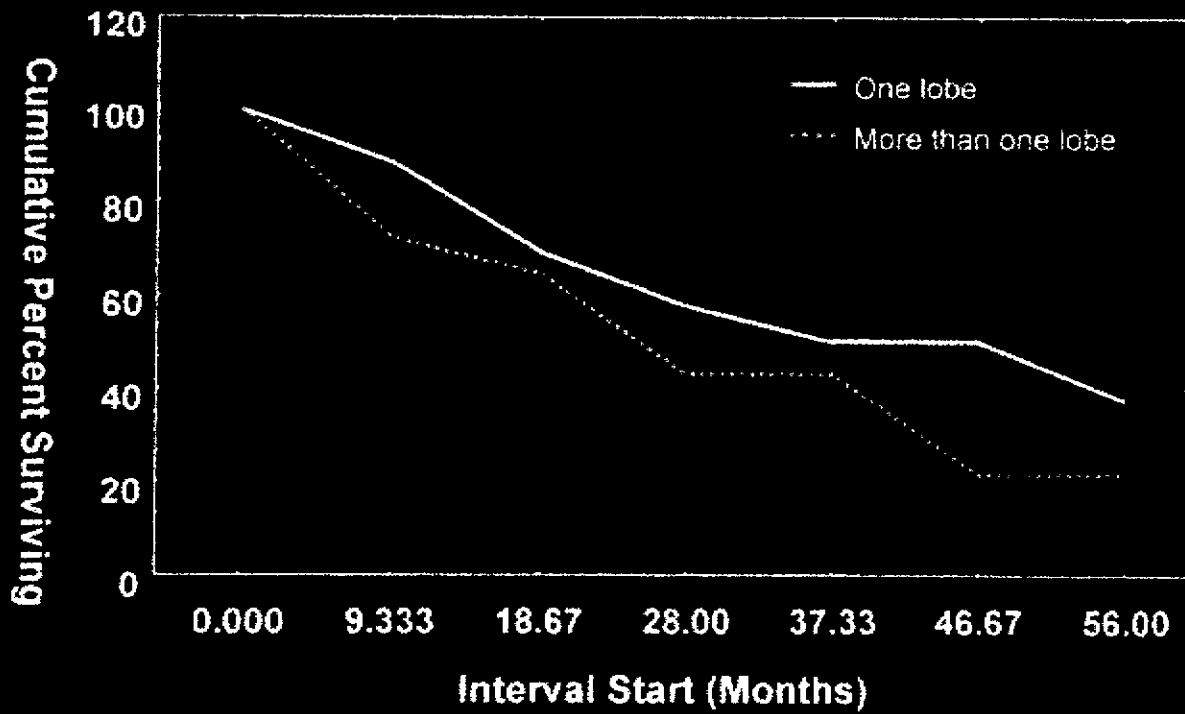
Discussion : (1)

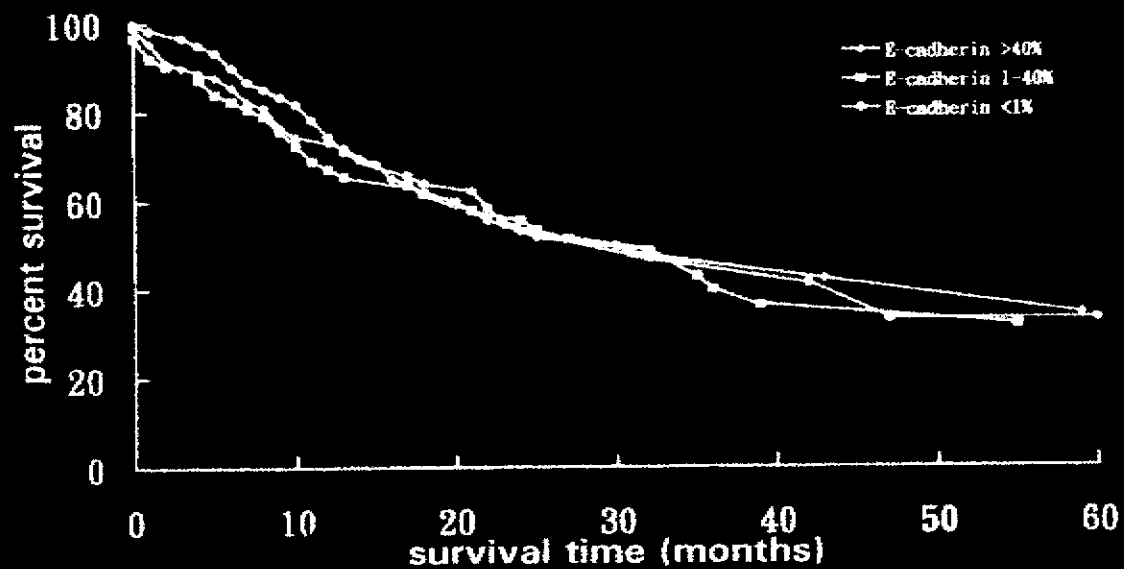
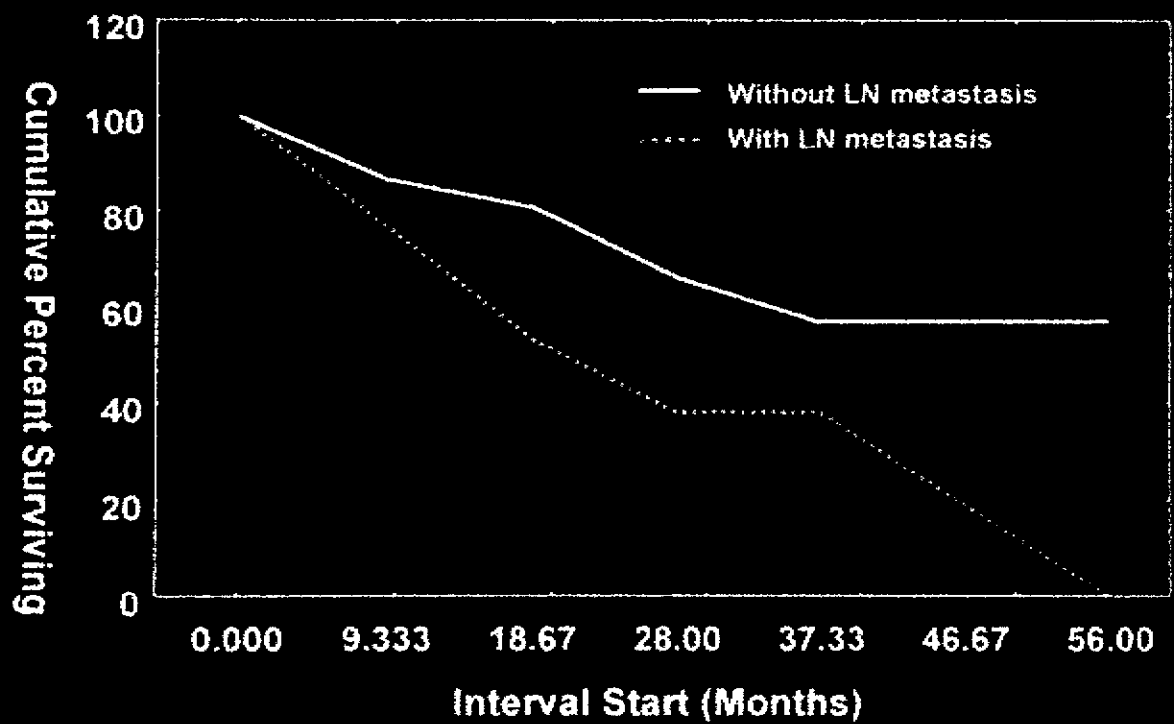
- Multifocal involvement is not unusual in NSCLC, especially in histological types of adenocarcinoma and bronchioloalveolar carcinoma
- A deliberate pathological examination should be performed to detect these lesions

Discussion : (2)

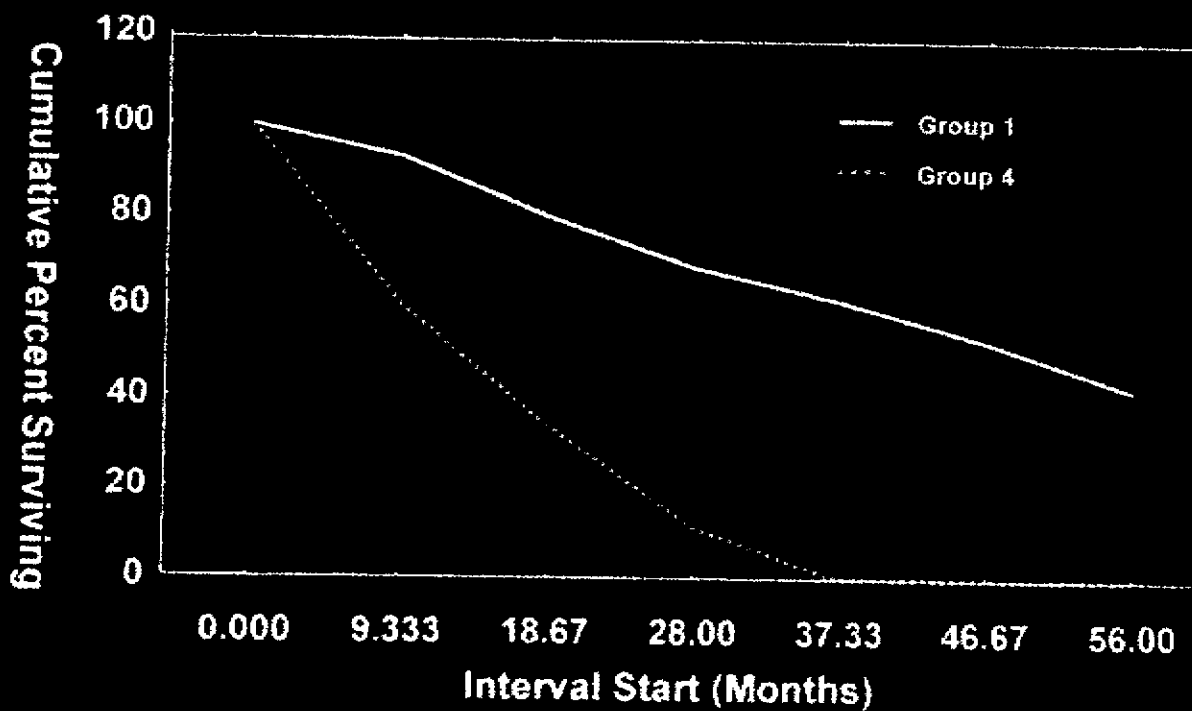
- Using the new TNM staging system to categorize these lesions to T4 or M1 may be improper, because their prognosis can be good if regional lymph nodes are negative for metastasis

Log-Rank Test $p=.08903$

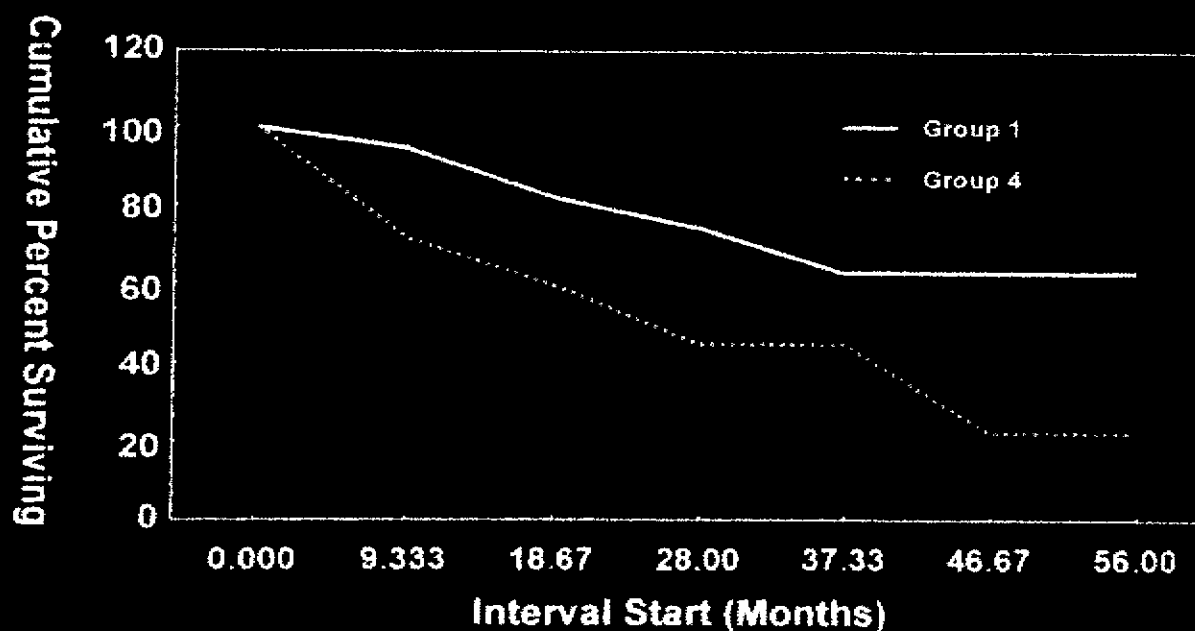




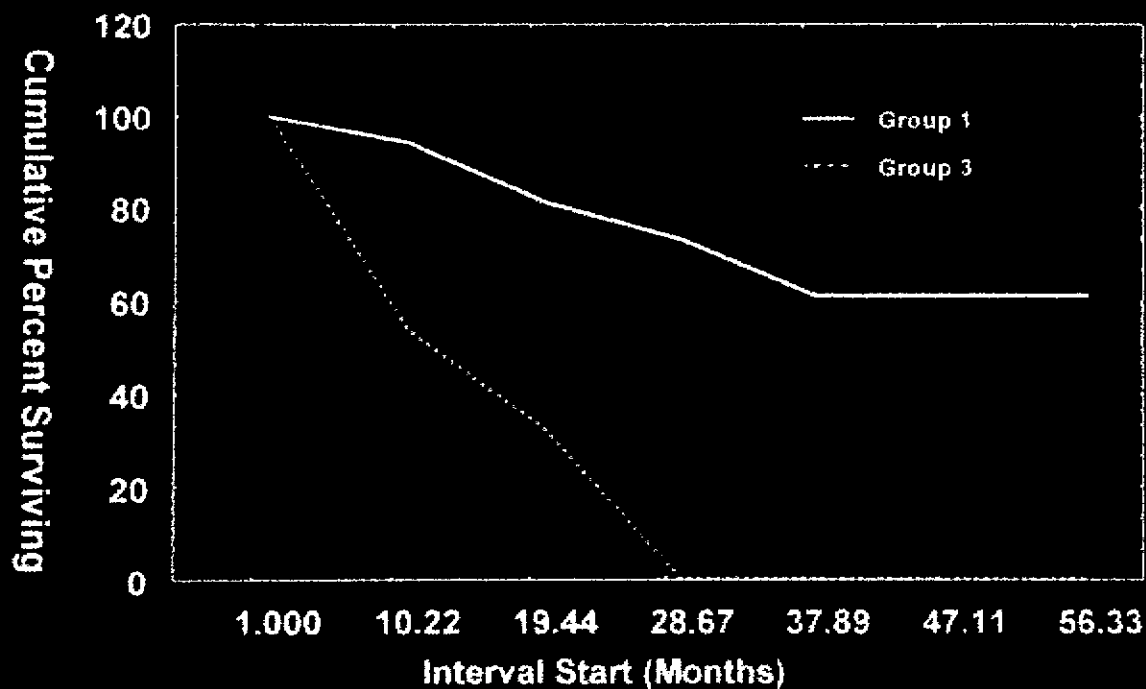
Relationship between p53 and survival (Log-Rank Test $p=.00467$)



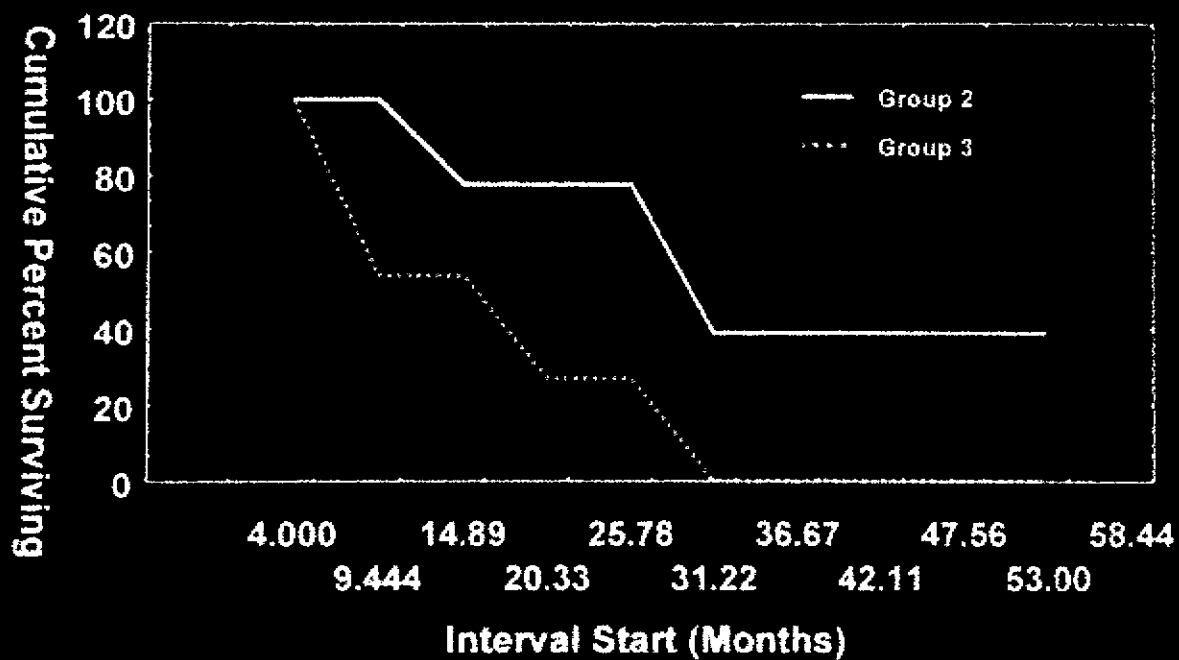
Relationship between Ki-67 and survival (Log-Rank Test $p=.04583$)



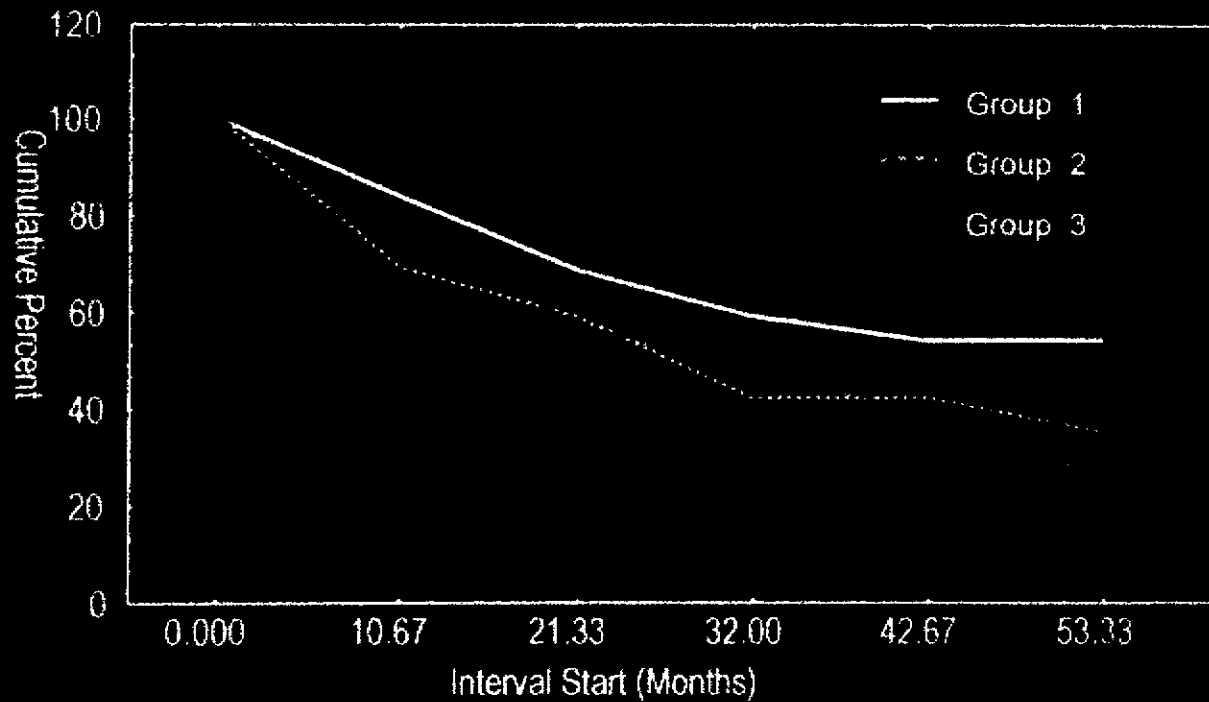
Relationship between Ki-67 and survival (Log-Rank Test $p=.00632$)



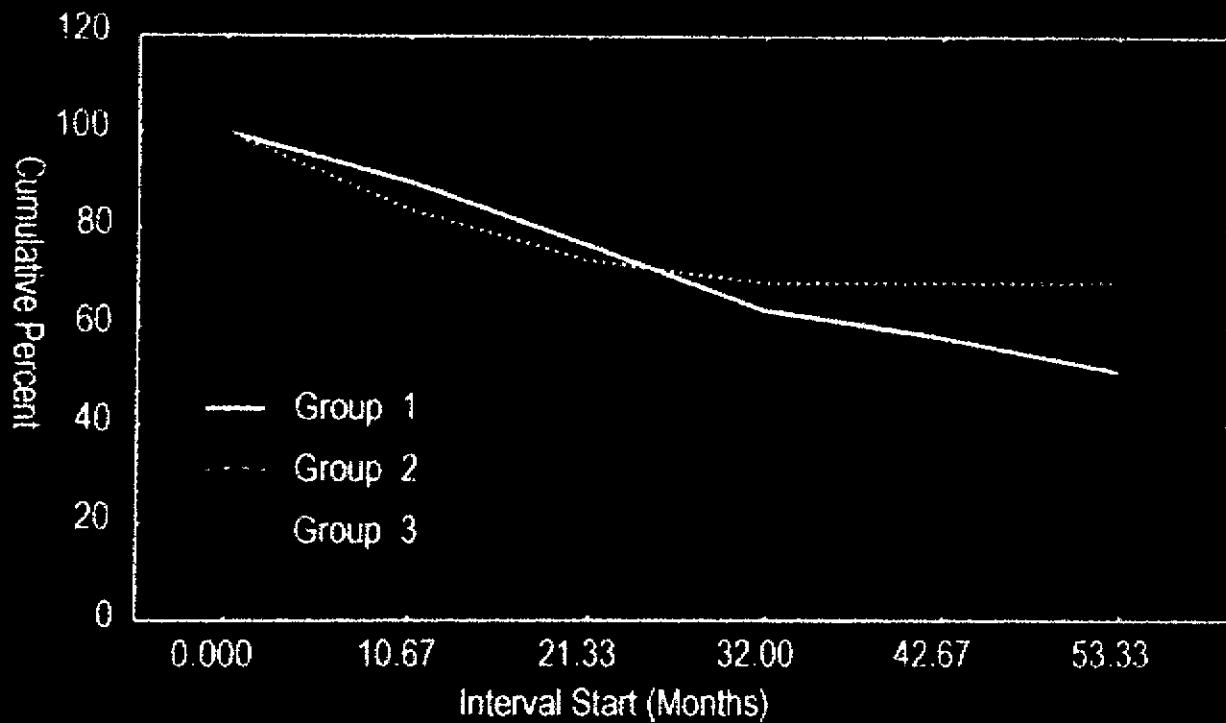
Relationship between Ki-67 and survival (Log-Rank Test $p=.02376$)



Relationship between Ki-67 and survival ($p = .13958$; $N = 207$)



Relationship between PCNA and survival ($p = .01547$; $N = 207$)



PCNA vs. Survival ($p = .00499$)

